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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

JOURNAL OF GENERAL CHEMISTRY OF THE USSR IN ENGLISH TRANSLATION

May, 1957

TABLE OF CONTENTS

	Page	Russ. Page
1. Investigation of Irrational Systems by the Method of Two Solvents. I.L. Krupatkin	1195	1113
2. Electron Diffraction Studies on Molybdic Heteropolyacids of Germanium. Z.F. Shakhova, G.N. Tishchenko and R.K. Motorkina	1200	1118
3. Complex Compounds of Tin. IV. T. Sumarokova and I. Litvyak	1207	1125
4. Enthalpies of Formation of Binary Compounds of the Elements of the Main Subgroup of Group V. The Phenomenon of Secondary Periodicity. S.M. Ariya, M.P. Morozova and S.A. Shchukarev	1213	1131
5. Polarographic Determination of 2,2'-Azobisisobutyronitrile, Aliphatic and Aromatic Nitriles. M.I. Bobrova and A.N. Matveeva	1219	1137
6. Radical and Ion Mechanism of the Alkylation of the Aromatic Nucleus. V. Benzylation of Naphthalene. I.P. Tsukervanik and G.S. Semeshko	1225	1143
7. Investigations in the Naphthalene Series. XV. The Rearrangement of Aromatic Sulfo Salts; Conversion of the Dry Salts of 2-Naphthylamine-1-Sulfonic Acid and 2-Naphthylsulfamic Acid. V.V. Kozlov	1229	1146
8. Investigations in the Naphthalene Series. XVI. The Conversion of the Salt of 2-Naphthol-6-Sulfonic Acid into the Salt of 2-Naphthol-7-Sulfonic Acid. V.V. Kozlov and G.G. Yakobson	1238	1156
9. The Nitration of Easily-Nitrated Aromatic Compounds. R.A. Slavinskaya	1243	1160
10. Investigations in the Field of Conjugated Systems. LXXIV. The Infrared Spectra and Reactivity of Vinylacetylene Hydrocarbons. A.A. Petrov, Yu.I. Porfiryeva and G.I. Semenov	1250	1167
11. Investigations in the Field of Conjugated Systems. LXXV. The Interaction of Propargylbromide with Aliphatic Aldehydes Under the Conditions of the Reformatsky Reaction. A.A. Petrov, Yu.I. Porfiryeva and G.I. Semenov	1258	1175
12. The Mechanism of the Conversions of Tertiary Alcohols of the Cyclopropane Series Under the Influence of Mineral and Organic Acids. VI. The Reaction of Methylethynylcyclopropylcarbinol With Sulfuric Acid and With Phosphorus Trichloride in the Presence of Pyridine. The Synthesis of Methyltrichloromethylcyclopropylcarbinol and the Investigation of its Reactions With Sulfuric Acid. T.A. Favorskaya and L.S. Bresler	1262	1179
13. Reaction of Cyclohexylacetylene With the Lower Saturated Monobasic Acids. A.I. Bolshukhin and A.G. Egorov	1268	1185
14. Investigation of Compounds Containing a Three-Membered Oxide Ring. XVII. Condensation of Chloroacetonitrile With Ketones. Synthesis of β,β'-Disubstituted Nitriles of Glycidic Acids. V.F. Martynov and A.V. Shchelkunov	1271	1188
15. Investigation of Compounds Containing a Three-Membered Oxide Ring. XVIII. Reaction of the Ethyl Ester of β-Tetramethyleneglycidic Acid With Aromatic Amines. V.F. Martynov.	1274	1191
16. Oxidative Breakdown of the Ozonide of Butadiene Rubber. A.I. Yakubchik, N.G. Kasatkina, G.I. Demidova and G.B. Federova	1278	1195

TABLE OF CONTENTS (continued)

Page Russ. Page

17. Alkylation in an Aqueous Medium in Presence of Quaternary Ammonium Salts. III. A.T. Babayan and M.G. Indzhikyan 1284 1201

18. Investigations of Glycol Ethers. XXX. Synthesis of Ethers of Dimethyleneglycol. Shamkhal Mamedov and M.R. Kulibekov 1289 1206

19. Unsaturated Cyclic Hydrocarbons and Their Halogenated Derivatives. XXV. Interaction of Methylcyclohexadiene-1,3 With Hexabromoethane and Quinoline. N.A. Domnin and V.A. Cherkasova 1296 1214

20. The Problem of the Electronic Structure and Reactivity of Free Radicals. V.V. Razumovsky 1298 1215

21. Heterocyclic Compounds. 56. The Action of Primary Amines Upon Propenylisopropenyl Ketone. I.N. Nazarev and N.I. Shvetsov 1300 1218

22. Investigation on Oxido Compounds. VIII. Interaction of α-Oxides of Allyl Ethers of o-, m- and p-Nitrophenols With Diethylamine. I.I. Chizhevskaya and V.I. Pansevich-Kolyada 1305 1223

23. Investigations of Unsymmetrical Organic α-Oxides. XIV. Transformations of Piperylene Monoxide. F.G. Ponomarev, O.G. Kharenko and M.F. Shavkova 1309 1226

24. Preparation of Phenols by Catalytic Condensation of Acetone With Acetylacetone. IV. B.N. Dolgov, L.V. Mozzhukhina and T.V. Nizovkina 1314 1231

25. Preparation of Phenols by Catalytic Condensation of Acetone With a β-Ketoalcohol (Cyclocondensation). V. B.N. Dolgov, L.V. Mozzhukhina and T.V. Nizovkina . . . 1317 1233

26. Catalytic Transformations of Ethyl Acetate Under Pressure. B.A. Bolotov and S.N. Borisov 1321 1237

27. Synthesis of Polymethyldimethylsiloxanes. K.A. Andrianov and V.M. Mantrova 1326 1243

28. Synthesis of Thiosemicarbazones and m-Iodobenzhydrazones of Some Halogenated Benzophenones. E.S. Novikova and L.A. Egorshina 1332 1249

29. Dialkylamides of Trichlorophosphazosulfuric Acid and Chlorides of N,N-Dialkylsulfamido-N'-Phosphoric Acid. A.V. Kirsanov and Z.D. Nekrasova 1335 1253

30. The Mechanism of the Gas-Phase Catalytic Reaction of Acetylene and Acetic Acid. R.M. Flid and A.V. Chirikova 1338 1256

31. Catalytic Rearrangements of Some Acetylated Arylamines. B.I. Ardashev and V.I. Minkin 1343 1261

32. Reduction of Naphtholcarboxylic Acids. I. Preparation of 1-Hydroxy-2-Naphthaldehyde. L.N. Lavrishcheva, N.M. Przhiyalgovskaya, S.A. Voitkevich and V.N. Belov 1346 1264

33. Reduction of Naphtholcarboxylic Acids. II. Synthesis of 2,3-Tetralonecarboxylic Acid and its Decomposition to β-Tetralone. N.M. Przhiyalgovskaya, L.N. Lavrishcheva and V.N. Belov 1349 1266

34. Synthesis of Mercaptoamino Compounds. I. Synthesis of 11-Amino-10-Hydroxyundecanoic Acid and Related Compounds. Yu.V. Markova, K.K. Kuzmina and M.N. Shchukina 1353 1270

35. Synthesis of Mercaptoamino Compounds. II. Synthesis of 11-Amino-10-Mercaptoundecanoic Acid and Related Compounds. Yu.V. Markova, K.K. Kuzmina and M.N. Shchukina 1357 1274

TABLE OF CONTENTS (continued)

	Page	Russ. Page
36. Synthesis With 1,1,3,3-Tetraalkoxypropanes. Preparation of the Simpler Heterocyclic Compounds. T.V. Protopopova and A.P. Skoldinov	1360	1276
37. Preparation of 2,3-Dimercaptopropanol, Containing Radioactive Sulfur. An.N. Nesmeyanov, A.B. Silaev and V.M. Fedoseev	1364	1280
38. Study of the Conditions and Mechanism for the Synthesis of Phosphorylcholine, Containing P^{32}. A.B. Silaev, An.N. Nesmeyanov and V.M. Kutyurin	1367	1283
39. Synthesis and Properties of Trisubstituted α-Naphthylsilane Derivatives. P.S. Sanin	1371	1286
40. Synthesis of Some Fluorine-Containing β-Aryl-β-Alanines. V.P. Mamaev	1376	1290
41. Models of the Protein Microstructure. I. Synthesis of N-Aminoacyl Derivatives of Phenylalanine Anhydride. L.N. Akimova	1380	1294
42. Some of the Properties of N-Benzylated Peptides. I. L.N. Akimova and N.I. Gavrilov.	1385	1299
43. Intramolecular Hydrogen Bonding and Ultraviolet Absorption Spectra. V. The Influence of Acids on the Electronic Spectra of Aminoacetophenones. A.E. Lutsky and V.V. Dorofeev	1389	1303
44. Dihydrosarcomycin and Related Compounds. I. A.B. Arendaruk, E.I. Budovsky, B.P. Gommikh, M.Ya. Karpeisky, L.I. Kudryashov, A.P. Skoldinov, N.V. Smirnova, A.Ya. Khorlin and N.K. Kochetkov	1398	1312
45. Halogenation of Aromatic Silanes. IV. Preparation and Properties of Chloro and Bromo Derivatives of p-Tolyltrichlorosilane. G.V. Motsarev and A.Ya. Yakubovich.	1404	1318
46. The Reaction of Diazo Compounds With Sulfamic Acid and its Derivatives. V. Reactions of Diazo Compounds With N-Phenylsulfamic Acid. D.Z. Zavelsky and L.A. Lishnevskaya	1414	1330
47. The Reaction of Diazo Compounds With Sulfamic Acid and its Derivatives. VI. The Indicator Properties of 4-Aminoazobenzene-N-Sulfonates. D.Z. Zavelsky and L.A. Lishnevskaya	1422	1339
48. Synthesis of Thiazolidone Derivatives of Biological Interest III. Condensation of Monochloroacetic Acid With Thiosemicarbazones in the Presence of Aldehydes. E.V. Vladzimirskaya	1427	1345
49. Synthesis of Thiazolidone Derivatives of Biological Interest. IV. Ultraviolet Absorption Spectra of p-Acetaminobenzylidene Derivatives. M.M. Turkevich and E.V. Vladzimirskaya	1430	1348
50. Reaction of 1-Chloro-3-Nitro-4-Hydroxyisoquinoline With Ammonia. V.N. Zelman and G.Ya. Vanag	1435	1353
51. Reaction of 2-Bromo-2-Phenylindanedione-1,3 With Amines. G.Ya. Vanag and A.K. Aren.	1440	1358
52. Complex Compounds of Monovalent Copper Salts With Various Addenda. M.M. Azanovskaya	1445	1363
53. Mixed Esters of Tert-(1,1,1-Trichloro)-Butyl-1-Trichloromethylcyclohexyl-1-Phosphorus Acid. II. V.S. Abramov and V.K. Khairullin	1447	1365
54. Investigation of Furan Compounds. IX. Synthesis and Hydrogenation of Tertiary γ-Furylalkanols. A.A. Ponomarev, Z.V. Til, A.D. Peshekhonova and V.P. Reshetov.	1451	1369

TABLE OF CONTENTS (continued)

Page Russ. Page

55. The Synthesis of 1-(4'-Sulfophenyl)-3-Methyl-5-Pyrazolone From the Sodium Salt of Acetoacetic Acid. P.A. Levin 1456 1374

56. Conversion of Terpenocyclohexanones into Formylterpenocyclohexanes, Terpeno-ε-caprolactones and Terpeno-ε-caprolactams. V.N. Belov and L.A. Kheifits. 1459 1377

57. A New Synthesis of Irone. V.N. Belov, N.A. Daev, S.D. Kustova, K.V. Leets, S.S. Poddubnaya, N.I. Skvortsova, E.I. Shepelenkova and A.K. Shumeiko. 1465 1384

58. Esters of 4(5)-Nitroimidazole-5(4)-Carboxylic Acid. L.P. Kulev and A.M. Rozhkov. . 1470 1389

59. Some Ethers of 4(5)-Hydroxymethylimidazole. L.P. Kulev and L.L. Skripova. 1473 1392

60. Fluorine-Containing Derivatives of Dimethylaminoazobenzene. L.M. Yagupolsky and M.S. Marenets. 1477 1395

61. Some N-Substituted β-Chloropropionamides. N.K. Kochetkov and N.V. Dudykina . . 1481 1399

INVESTIGATION OF IRRATIONAL SYSTEMS BY THE METHOD OF TWO SOLVENTS

I.L. Krupatkin

The two-solvent method previously proposed [1] consists of the investigation of a reacting liquid system by phase-separation in two solvents – polar and nonpolar. It has been found that this permits studying the details of the chemical reaction in the system, the effect of a solvent on it, and the nature of the properties of the compounds that are formed. By this means also, conditions are established for the investigation of systems with an abnormal indication of chemical affinity on the phase separation surfaces. In previous work along this line [1] the applicability of this method to binary rational systems was demonstrated. The further development of the two-solvent method raised the question of its application to binary irrational systems. The solution of this problem was the goal of the present work. For this purpose the reaction between phenol and antipyrine was studied in the strongly polar solvent water and in the nonpolar solvent ligroin. Thus, two ternary systems were chosen as the subjects of investigation by the phase separation procedure: phenol-antipyrine-ligroin and phenol-antipyrine-water.

EXPERIMENTAL

The following materials were used for the investigation: pharmacopeia grade antipyrine with m.p. 113°, freshly distilled phenol with m.p. 42°, a ligroin fraction boiling within the limits 120-140°, and twice-distilled water. The work was carried out by the visual-polythermal method of V.F. Alekseev [2]. Sealed glass ampoules containing the mixtures under investigation were placed in an oil thermostat. For the investigation of the three-component systems a study was made of polythermal sections through their temperature-concentration prisms, passing from the water (or ligroin) edge to the face of the predominant binary phenol-antipyrine system.

The binary systems comprising the ternary systems studied had the following characteristics. The phenol-antipyrine system was subjected to a fusion study [3]. In this system one chemical compound was found, which melted at 55.5° and contained 33.33% of phenol (molecular ratio of the components of the system 1 : 1). This compound was a product of salt formation in the system, since antipyrine is a monoacid base and phenol acts as a monobasic acid. The system phenol-water was investigated by phase-separation and fusion methods [4]. In this system a stable phase-separation curve was found with an upper critical point occurring at 66° and 34% phenol content. In the present work, this system played the part of a homogeneous system, since the study of the ternary systems was carried out above 66°. The antipyrine-ligroin system was studied by phase-separation [1]. In this system a stable phase-separation curve with a very high critical point was found. Antipyrine was infinitely soluble in water. Phenol separated with ligroin at low temperatures, therefore this system here played the role of a homogeneous system. The upper part of the stable phase-separation curve for this system was studied in the present investigation (Table 1). Its upper critical point corresponded to 20° and 42% of ligroin.

TABLE 1

Equilibrium in the System Phenol-Ligroin

Ligroin (wt. %)	Temperature of phase-separation
53.22	18.0°
31.37	19.0
41.74	20.0

In the ternary system phenol-antipyrine-ligroin five sections were studied. The numerical data obtained from the sections are given in Table 2 and the phase-separation polytherms themselves are shown in Figure 1. The latter are curves that rise sharply from their extremities and have flatly sloping maxima in their central parts. In sections 1 and 2 the maxima were not reached because they were located at high temperatures. The form of the phase-separation polytherms indicated that in mixtures at the extremities of the curves the mutual solubility of the liquid phases had little dependence on the temperature; on the contrary in the central portions of the curves the solubility increased rapidly with a rise in the temperature. Thus, for example, in section 4 in the ligroin corner a rise in temperature of 25° increased the mutual solubility of the liquids by 5% in all, but in the central part of this polytherm a total temperature rise of 2° increased the solubility by 35%.

TABLE 2

Equilibrium in the System Phenol-Antipyrine-Ligroin

Section 1: 20% phenol, 80% antipyrine		Section 2: 33% phenol, 67% antipyrine		Section 3: 50% phenol, 50% antipyrine	
Ligroin (wt. %)	Temperature of phase-separation	Ligroin (wt. %)	Temperature of phase-separation	Ligroin (wt. %)	Temperature of phase-separation
6.54	68.0°	9.09	77.0°	11.50	79.0°
10.71	101.0	15.37	113.0	14.70	93.0
21.37	143.0	17.67	119.0	24.81	121.0
80.00	154.0	25.72	141.0	39.76	135.0
90.00	118.0	80.07	149.0	60.00	134.0
95.04	100.0	90.08	116.0	80.00	125.0
		95.00	88.0	90.00	115.0
				95.00	82.0

Section 4: 67% phenol, 33% antipyrine		Section 5: 80% phenol, 20% antipyrine	
Ligroin (wt. %)	Temperature of phase-separation	Ligroin (wt. %)	Temperature of phase-separation
12.43	54.0°	24.81	66.0°
21.67	87.0	40.68	76.0
29.23	97.0	48.34	78.5
50.00	106.0	50.24	78.0
64.87	107.0	55.47	79.0
80.74	107.0	70.02	80.0
90.00	97.0	80.22	75.5
95.00	71.0	84.96	73.0

From the polytherms obtained five phase-separation isotherms were constructed for the ternary system phenol-antipyrine-ligroin, shown in Figure 3. All of the isotherms represent curves running from solubility breaks of the antipyrine-ligroin system into the prism of the ternary system. Consequently, at the temperatures investigated in this ternary system phenol plays the role of a homogenizer. In the isotherms for 70, 100 and 120° there occur irrational maxima of mutual solubility of the liquid phases. At 70° and 100° in the binary phenol-antipyrine system they fit at the composition of the compound recorded in the fusion diagram. In the 120° isotherm the solubility maxima are very diffuse and in the 135 and 150° isotherms they are entirely absent. This indicates on the one hand that the phenol-antipyrine system actually is irrational. On the other hand, it appears that the compound of the phenol-antipyrine system undergoes thermal dissociation in the liquid phase of the ternary system in question and above 120° it is completely dissociated. As shown in Figure 3, at the temperatures studied in the ternary system depicted, the phase-separation surface borders on the side of the binary antipyrine-ligroin system. On lowering the temperature it approaches more and more to the side of the binary phenol-ligroin system and below 20° it must join it.

In the ternary phenol-antipyrine-water system five sections were studied. The data obtained are given in Table 3, and the phase-separation polytherms are shown in Figure 2. All the polytherms have flat maxima and rise sharply upward from their extremities. The polytherms of sections 3 and 4 almost coincide. The maxima of the polytherms increase from sections 1 to 3, remain at the same temperature in 3 and 4, and decrease to section 5. In the water corner all the polytherms approach each other very closely.

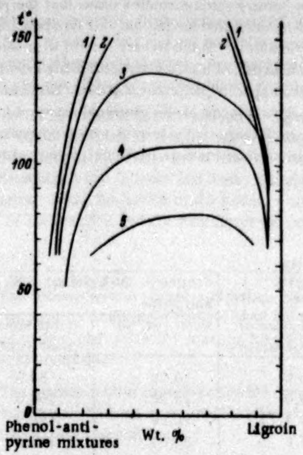

Fig. 1. Polytherms of phase-separation for the ternary system phenol-antipyrine-ligroin. Explanation in the text.

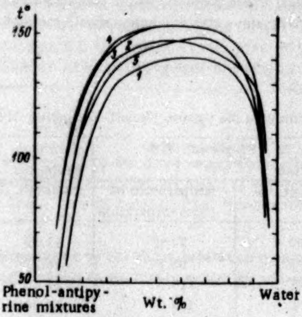

Fig. 2. Polytherms of phase-separation for the ternary system phenol-antipyrine-water. Explanation in the text.

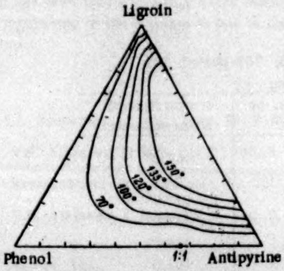

Fig. 3. Isotherms of solubility in the ternary system phenol-antipyrine-ligroin.

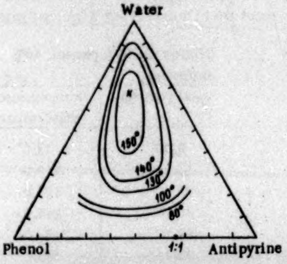

Fig. 4. Isotherms of solubility in the ternary system phenol-antipyrine-water.

From the polytherms obtained five phase-separation isotherms were constructed for the ternary system phenol-antipyrine-water, shown in Figure 4. The isotherms are closed curves, concentrically decreasing with increasing temperature. Thus, in this ternary system there exists an upper, triple, critical point (k); the latter occurs at 153° and a composition of 60% water, 22% phenol and 18% antipyrine. As Figure 4 shows, in the ternary system depicted at the temperatures studied the phase-separation surface is located within its temperature-concentration prism between the water edge and the face of the binary phenol-antipyrine system. At lower temperatures this surface must join the face of the binary separating system phenol-water. All the isotherms have minima of mutual solubility of water and the liquid mixtures of phenol with antipyrine. The upper triple critical point and the minima of the isotherms occur in the binary phenol-antipyrine system not at the composition of the compound, but at an irrational composition – 55.55% phenol and 44.45% antipyrine, in which the molecular ratio of these components is 2.5 : 1.

Comparison of the phase-separation isotherms of the two ternary systems studied shows that the presence in the liquid phase of the compound of the binary system phenol-antipyrine having the 1:1 composition is registered in the ternary system with ligroin by irrational solubility maxima. In the ternary system with water the compound referred to is abnormally reflected because of the formation of a secondary, difficultly soluble complex of irrational composition, which explains the genesis of the upper, triple, critical point. This also demonstrates that the two-solvent method is reliable for elucidating the character of the chemical reaction in binary, irrational, liquid systems. In the case under consideration, by replacing a polar solvent with a nonpolar one an irrational system with an abnormal reflection of the reaction is converted into an irrational system with a normal reflection.

TABLE 3

Equilibrium in the System Phenol-Antipyrine-Water

Section 1: 28% phenol, 72% antipyrine		Section 2: 33% phenol, 67% antipyrine		Section 3: 50% phenol, 50% antipyrine	
water (wt. %)	temperature of phase-separation	water (wt. %)	temperature of phase-separation	water (wt. %)	temperature of phase-separation
15.00	71.0*	12.69	80.0*	10.00	80.0*
20.09	98.0	18.27	109.0	15.00	108.0
25.13	114.5	31.58	139.0	20.20	126.0
35.00	132.0	50.00	147.0	30.00	143.0
45.11	137.0	70.00	145.5	20.14	150.0
59.87	141.0	80.00	140.0	49.86	153.0
70.00	140.0	90.00	132.0	60.00	153.0
80.05	137.0	95.00	103.0	68.05	153.0
90.00	121.0			90.07	138.0
95.00	77.0			93.00	
				96.00	72.0

Section 4: 60% phenol, 40% antipyrine		Section 5: 70% phenol, 30% antipyrine	
water (wt. %)	temperature of phase-separation	water (wt. %)	temperature of phase-separation
9.06	73.0*	10.11	57.0*
15.00	110.0	15.00	91.0
20.00	127.0	20.00	112.0
30.00	144.0	25.00	122.0
40.10	150.5	35.59	138.0
55.14	153.0	50.08	145.0
65.00	153.0	60.00	147.5
74.88	152.0	70.00	149.0
85.00	144.0	80.00	145.0
95.00	90.0	90.00	127.0
		95.04	94.0

The ternary system phenol-antipyrine-water is composed of substances with strongly hydrating functional groups and water. Consequently, in this system hydration processes predominantly appear. The strong reaction of antipyrine with water results in its infinite solubility. The reaction of phenol with water is somewhat decreased because of the presence in the system of a region of phase separation between them at lower temperatures. The strong hydration, which is unequal for the components, leads to the instability of the 1:1 compound in the ternary system and the formation of a complex with a greater phenol content. The hydration processes in the system cannot completely eliminate the reaction of the phenol with the antipyrine. Partial loss of their acid and basic functions upon formation of the complex leads to a decrease in hydration, and consequently to a lesser solubility of the complex in water. This is reflected in the phase-separation isotherms as solubility minima which necessitate

*Figure obscured in Russian text – Publisher.

the emergence of an upper, triple, critical point. Thus, the chemical and phase equilibria in liquid systems are closely related to each other and are mutually dependent; hence all the component binary systems of a given ternary system influence each other. A weakening of the reaction in one of them leads to a strengthening of the reaction in the remaining component binary systems.

In the ternary system phenol-antipyrine-ligroin hydration processes are absent and the 1:1 compound present in the liquid phase of the ternary system is normally reflected in the phase-separation isotherms. Here at reduced temperatures the compound is fixed by association processes. However, upon raising the temperature thermal dissociation sets in more and more, and above 120° the compound is not detected in the phase-separation isotherms. Thus, the nature of the solvant exerts a strong influence on the reacting system, changing the character of the reaction and the stability of the compounds formed.

SUMMARY

1. The ternary system phenol-antipyrine-ligroin has been investigated by the phase-separation method. In the phase-separation isotherms a compound of the predominant system phenol-antipyrine with 1:1 composition is reflected in irrational solubility maxima that disappear above 120°. This indicates thermal decomposition of the chemical compound.

2. The ternary system phenol-antipyrine-water has been investigated by the phase-separation method. It involves the systems with an upper, triple, critical point. The latter occurs in the binary system phenol-antipyrine at an irrational composition.

3. In the investigation of the two ternary systems referred to, the binary irrational system phenol-antipyrine has been studied by the two-solvent method. The applicability of this method to the study of reaction in liquid, binary, irrational systems has been demonstrated. The nature of the effect of solvents of different polarity on the reacting binary system phenol-antipyrine has been clarified.

4. It has been shown that in a liquid ternary system the component binary systems mutually affect each other. A weakening of the reaction in one of them leads to a strengthening of the reaction in the other two binary systems.

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ELECTRON DIFFRACTION STUDIES ON MOLYBDIC HETEROPOLYACIDS OF GERMANIUM

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The literature contains descriptions of the following heteropoly compounds containing germanium as the central atom and radicals of molybdenum oxides as addenda: germanomolybdic heteropolyacid $H_8[GeMo_{12}O_{40}]$ [1], germanovanadomolybdic heteropolyacid $H_8[GeMo_{10}V_2O_{40}]$ [2] and germanomolybdenum "blue" [3, 4] whose structure has not been ascertained. This last compound has not been isolated as a chemical individual. All three of the compounds listed find application in analytical chemistry for the quantitative determination of germanium. Colorimetric methods based on the use of their intense colors (yellow, orange and blue respectively) are among the most accurate and easy methods for the determination of this element.

The similarity in the conditions for the formation of the above complexes in solution, in the conditions for their separation in the solid state and also in a number of their chemical properties is so great that the only explanation is that their structures, which up to the present cannot be said to have been fully studied, are fully analogous. An explanation of the structural analogy between these compounds will at the same time make it possible to unify a number of analytical methods based on their use. One of the most confused and contradictory problems in inorganic and analytical chemistry is that concerning the composition and structure of the blue products of the reduction of molybdenum heteropoly compounds.

In spite of the results of the latest studies [5-9] which assert that on reduction of the heteropoly compounds no decomposition of the complex anion takes place, a number of authors still consider that the blue color of the reduction products from the heteropoly compounds is caused by a mixture of colloidal molybdenum oxides formed by the decomposition of the original complexes [10, 15].

Weissberg and Dain [6, 7] have shown spectrophotometrically that the derivatives of the heteropolyacids of silicon, phosphorus and arsenic are structurally similar to one another and to the unreduced complexes.

We have reached similar conclusions in a study of the absorption spectra of the germanium heteropolyacids – germanomolybdic, germanovanadomolybdic and germanovanadotungstic acids and their reduction products. The work was carried out using an SF-4 spectrophotometer in the wavelength range from 220 to 1100 mμ. It was established that all the germanium heteropoly compounds studied have an extremely high light absorption in the ultraviolet region of the spectrum and that the absorption falls rapidly with increasing wavelength.

The heteropolyacids containing molybdenum oxide radicals as addenda (germanomolybdic and germanovanadomolybdic) have no maxima of light absorption in the range of wavelengths indicated. Their maxima of light absorption probably lies further into the short wave region of the spectrum, which is not attainable with the SF-4 spectrophotometer. The replacement of two atoms of molybdenum by vanadium in the molecule of germanomolybdic heteropolyacid is not reflected in the general character of the light absorption of these compounds, merely increasing it in the visible region of the spectrum.

In contrast to those of the molybdenum heteropolyacids, the light absorption curves of germanotungstic and germanovanadotungstic heteropolyacids have well-defined maxima in the 260-265 mμ region.

Study of the absorption of the blue reduction products of all the heteropolyacids mentioned has shown that the absorption spectra of the "blues" in the ultraviolet region is analogous to the spectra of the original heteropoly compounds. In the case of the tungsten heteropolyacids of germanium the light absorption maximum in the

260-265 mμ region is preserved after their conversion into the "blue." In the visible region the spectra of all the "blues" studied differ essentially from the spectra of the original heteropolyacids by the presence of a maximum of light absorption at 835 mμ. The presence of this second maximum on the light absorption curve is evidently related to the intensification of polarization phenomena on reduction of the complex.

The presence of a well-defined maximum in the ultraviolet region of the spectrum of the tungstic "blues" at the same wavelength as for the unreduced heteropolyacids proves the general nature of the structure of the heteropolyacid and the heteropoly blue. From this it may be concluded that in the formation of the heteropoly blues the complex heteropolyanion is not decomposed; only a few of the atoms of the addenda are reduced in it while their distribution in space in preserved as it was in the original unreduced heteropolyacids. However, the spectrophotometric study enables this conclusion to be made chiefly for the tungsten heteropolyacids, since the absence of maxima on the light absorption curves for the molybdenum heteropolyacids in the 220-1100 mμ range makes it difficult to prove a similar analogy in the structures of the molybdenum heteropolyacids and their reduction products.

Inasmuch as it is just these molybdenum heteropolyacids which have the widest application in analytical chemistry, a proof of analogous structures for their yellow and blue forms would enable a whole series of practically important conclusions to be made.

It is well known that the methods for the determination of various complex-forming elements in the form of molybdenum "blues" are in the majority of cases empirical and difficult to reproduce, in spite of their ease and high sensitivity.

We therefore undertook an electron diffraction study of germanomolybdic and germanovanadomolybdic acids and of the "blue" obtained by the reduction of germanomolybdic heteropolyacid with Mohr's salt (ferrous ammonium sulfate) in the conditions used for the quantitative determination of germanium in the form of this complex.

EXPERIMENTAL

Solutions of individual specimens of the heteropolyacids, prepared by synthesis and purification from excess components, were used to obtain the electron diffraction patterns. The electron diffraction method of analysis was chosen by us since this makes it possible to study substances crystallized from very dilute solutions; films of 10^{-5}-10^{-6} mm thickness were studied.

In addition, the electron diffraction method of analysis has advantages over the x-ray method in the speed and ease of specimen preparation and in the shortness of exposures. The work was carried out on a vertical electron diffraction apparatus EM-4 of GOI construction. A detailed description of the instrument, the experimental technique of its use and the interpretation of the patterns, together with the theoretical principles of the method and the trends in its development are given in E.G. Pinsker's book [11].

Electron diffraction patterns were taken for the following substances: 1) germanomolybdic heteropolyacid, 2) germanovanadomolybdic heteropolyacid, 3) the "blue" obtained by the reduction of germanomolybdic heteropolyacid, 4) ammonium paramolybdate, 5) sodium paramolybdate, 6) normal sodium molybdate. The electron diffraction pattern for germanovanadomolybdenum "blue" was not taken, since this compound is rapidly oxidized in air, as a result of which there is considerable experimental difficulty attached to the recording of its electron diffraction pattern, and although it is of a certain interest, it has no great practical significance.

1. Preparation of the specimens. In the present work the specimens for electron diffraction study were prepared by crystallization from 0.25-0.5% aqueous solutions of individually synthesized heteropolyacid samples on to a celluloid support at a temperature of 50-60°.

The preparation of specimens of the substances studied was attended by a whole series of difficulties as a result of their relatively low stability on crystallization in air from dilute solutions. In addition, it was found that the usual method for preparing specimens of germanovanadomolybdic heteropolyacid did not give a well-defined diffraction pattern, evidently as a result of the breakdown of its lattice on removal of water of constitution in vacuo. For this reason the specimens used in the study were covered with a second layer of celluloid.

Ammonium and sodium paramolybdates and normal sodium molybdate, when crystallized onto a celluloid support from aqueous solutions in the cold or at raised temperatures, did not form films giving a good diffraction pattern, but separated either in the form of coarse crystalline formations, opaque to electrons (on rapid crystallization with heating to 80-90°), or in the form of an amorphous mass of molybdic acid, formed as a result of hydrolysis on very slow crystallization in the cold and giving diffuse, noncharacteristic rings on the electron diffraction pattern. When the sodium and ammonium molybdate specimens were being prepared, therefore, a few drops of ethyl alcohol, purified by distillation, were added to the celluloid support with the solution of the sample, after which the solvents were removed by heating to 60-70°. The addition of the alcohol reduced the surface tension of the aqueous molybdate solutions, the drops of these solutions flowed out in a thinner layer on the support, the mixture of water and alcohol evaporated more rapidly and the molybdate specimens were obtained in the form of crystalline films of the required thickness.

2. Description of the electron diffraction patterns. In the electron diffraction study of germanomolybdic (Figure 1) and germanovanadomolybdic (Figure 2) heteropolyacids, patterns were obtained from polycrystalline films, as is proved by the uniform density of all the rings and the absence of any change in the diffraction pattern on changing the angle between the surface of the specimen and the electron beam.

Fig. 1. Electron diffraction pattern for germanomolybdic heteropolyacid.

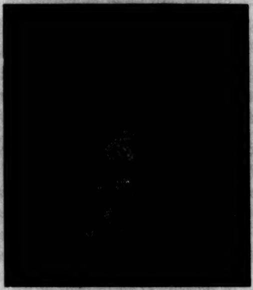

Fig. 2. Electron diffraction pattern for germanovanadomolybdic heteropolyacid.

Three types of electron diffraction pattern were obtained for germanomolybdenum heteropoly blue – that of the true polycrystalline layer (Figure 3), that of the textured polycrystal and an electron diffraction pattern with fine, densely packed lines, some of which belong to the heteropoly blue and some of which are obtained as a result of its decomposition into paramolybdate. It should be noted that paramolybdate lines are also sometimes observed in the electron diffraction patterns of germanomolybdic and germanovanadomolybdic heteropolyacids. The decomposition is evidently brought about by heating the specimens when crystallizing, and also by removal of water of crystallization in vacuo. Many of the lines in the electron diffraction patterns of such decomposed heteropolyacids are not identical with the lines of the paramolybdate and normal molybdate, and evidently belong to some other molybdenum anion. A more detailed study of these patterns will probably make it possible to explain the mechanism of decomposition of the molybdenum heteropolyacids.

We give for comparison the electron diffraction pattern of sodium paramolybdate from the orientated polycrystal (Figure 4) and the electron diffraction point diagram of normal sodium molybdate (Figure 5).

3. Comparison of the electron diffraction patterns of the various substances. It is clear from comparison of the electron diffraction patterns obtained that the patterns of germanomolybdic and germanovanadomolybdic acids and of germanomolybdenum blue have much in common in the disposition of the rings and in the alternation in line intensities, which indicates a similarity in the structures of these compounds. From a comparison of the electron diffraction patterns of the heteropolyacids and the molybdates it is seen that they have more differences than features in common, i.e., the paramolybdic anion and the heteropolyanion have completely different structures. We give below the results of indexing the electron diffraction patterns of the heteropolyacids (Tables 1-3). NH_4Cl was used as standard.

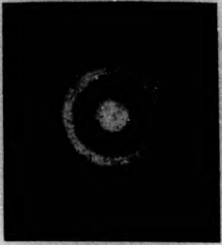

Fig. 3. Electron diffraction pattern of germanomolybdenum heteropoly blue.

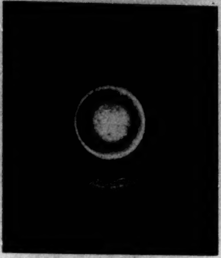

Fig. 4. Electron diffraction pattern for sodium paramolybdate.

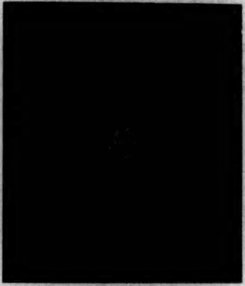

Fig. 5. Electron diffraction pattern for normal sodium molybdate.

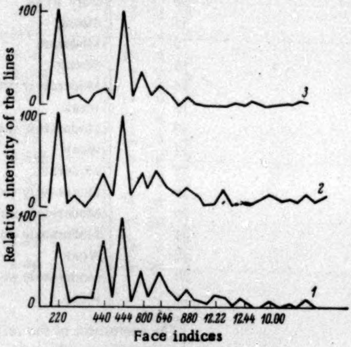

Fig. 6. A comparison of the experimental values of the intensities of the lines in the electron diffraction patterns of germanomolybdic heteropolyacid (1), germanovanadomolybdic heteropolyacid (2) and germanomolybdenum heteropoly blue (3).

A diagram showing a comparison of the experimental intensities of the reflections for germanomolybdic and germanovanadomolybdic heteropolyacids and for germanomolybdenum heteropoly blue is given in Figure 6. It is seen from the figure that the order of the intensities of the reflections for these three compounds is identical.

The density of germanovanadomolybdic heteropolyacid, according to the data of B.N. Ivanov-Emin [2], is d^{25} 2.60-2.65, from which the number of molecules in the unit cell is $Z = dv/Mmn = 8.3$. Probably $Z = 8$, which agrees with the literature data from the study of the highly hydrated forms of the heteropolyacids [13]. The value of the density obtained by calculation from the electron diffraction data is d_{el} 2.480.

As the results of indexing the electron diffraction patterns show, germanomolybdic and germanovanadomolybdic heteropolyacids and germanomolybdenum blue crystallize in cubic syngony and have very similar unit cell dimensions (23.05, 23.10 and 23.16 A respectively). If we take the unit cell dimensions as halved, then all the lines in the electron diffraction patterns obtained are indexed, except the first very weak line, for which $d = 9.40$ A. This line is evidently caused mainly or entirely by the presence of water of crystallization, since it is most clearly seen on the electron diffraction patterns obtained in conditions where the evaporation of water in vacuo was prevented – under a second layer of celluloid. The two-fold increase in the cell dimensions is evident-

TABLE 1

Germanomolybdic Heteropolyacid

Reflection No.	Intensity*	Value of d (in A)	hkl for a = = 23.05 A
1	Very very weak	9.40	2 1 1
2	Very strong	8.14	2 2 0
3	Weak	6.64	2 2 2
4	Moderately weak	5.75	4 0 0
5	Moderately weak	5.20	4 2 0
6	Moderately weak	4.70	4 2 2
7	Very strong	4.08	4 4 0
8	Weak	3.65	6 2 0
9	Very very strong	3.32	4 4 4
10	Very weak	3.08	6 2 4
11	Strong	2.88	8 0 0
12	Moderate	7.72	6 6 0
13	Strong	2.46	6 4 6
14	Moderately strong	2.26	8 6 2
15	Weak	2.14	10 4 0
16	Moderately strong	2.04	8 8 0
17	Weak	1.94	12 0 0
18	Moderate	1.87	12 2 2
19	Moderately weak	1.78	10 8 2
20	Moderately weak	1.74	12 4 4
21	Moderately weak	1.63	10 10 0
22	Weak	1.57	10 10 4
23	Moderately weak	1.465	12 10 2
24	Weak	1.42	10 10 8

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*The intensities of the reflections in the electron diffraction patterns in this and later cases was estimated visually on a nine-degree scale [11].

ly related to the increase in the number of molecules of water of crystallization, and removal of the excess leads to the pentahydrate structure with a = 11.50-11.60 A [14].

The values of the unit cell dimensions obtained by us for the molybdenum heteropolyacids of germanium are similar to the literature data for the highly hydrated forms of heteropolyacids and their salts. Illingworth and Keggin [12] point out that silicomolybdic heteropolyacid gives an x-ray diffraction pattern analogous to the x-ray diffraction pattern of the 29-hydrate of phosphotungstic heteropolyacid, for which a = 23.28 A [13]. It has been established by Keggin that on dehydration of silicomolybdic heteropolyacid with the aim of obtaining the pentahydrate, whose structure should be analogous to the structure of $H_3PW_{12}O_{40} \cdot 5H_2O$ with a = 12.14 A, the structure breaks down, giving hexagonal crystals of a completely different type. A whole series of salts of molybdenum heteropolyacids of phosphorus studied by Ferrari and coworkers [14] has unit cell dimensions similar to the values obtained (a = 23.10-23.20 A), although many of the salts of the heteropolyacids studied have unit cell dimensions which are half these values (a = 11.70-11.90 A) and these crystallize in the same way as the pentahydrate of phosphotungstic heteropolyacid. It has been established, however, that heteropolyacids are, as a rule, more extensively hydrated than their salts. This is also evident from an examination of the structures: the larger the ions of the metal replacing the hydrogen ions of the heteropolyacid, the fewer molecules of water of crystallization are able to fit into the empty spaces in the structure between the $MoO_6(WO_6)$ octahedra. Thus, the results obtained by us agree with the literature data on structural studies of heteropoly compounds.

The similarity in the diffraction patterns of germanomolybdic and germanovanadomolybdic acids and germanomolybdenum blue, together with the similarity in unit cell dimensions, indicate that these compounds have

TABLE 2

Germanovanadomolybdic Heteropolyacid

Reflection No.	Intensity	Value of d (in A)	hkl for a = = 23.10 A
1	Very weak	9.40	2 1 1
2	Very very strong	8.16	2 2 0
3	Moderate	5.77	4 0 0
4	Moderate	4.71	4 2 2
5	Strong	4.09	4 4 0
6	Moderately weak	3.65	6 2 0
7	Very very strong	3.33	4 4 4
8	Moderately weak	3.084	6 2 4
9	Strong	2.88	8 0 0
10	Moderately strong	2.72	8 2 2
11	Strong	2.46	6 4 6
12	Moderately strong	2.27	8 6 2
13	Moderate	2.15	10 4 0
14	Moderately strong	2.046	8 8 0
15	Moderate	1.93	12 0 0
16	Moderately strong	1.76	10 8 2
17	Weak	1.74	12 4 4
18	Weak	1.665	8 8 8
19	Moderate	1.63	10 10 0
20	Weak	1.59	14 4 0
21	Weak	1.57	10 10 4
22	Weak	1.47	12 2 10
23	Weak	1.44	10 10 8

TABLE 3

Germanomolybdenum Blue

Reflection No.	Intensity	Value of d (in A)	hkl for a = = 23.16 A
1	Very weak	9.4	2 1 1
2	Very very strong	8.16	2 2 0
3	Weak	6.65	2 2 2
4	Moderately weak	5.77	4 0 0
5	Moderate	4.72	4 2 2
6	Moderately strong	4.08	4 4 0
7	Weak	3.66	6 2 0
8	Very very strong	3.33	4 4 4
9	Moderately weak	3.08	6 2 4
10	Strong	2.89	8 0 0
11	Moderately weak	2.73	6 6 0
12	Moderately strong	2.46	6 4 6
13	Moderate	2.27	8 6 2
14	Moderately weak	2.04	8 8 0
15	Very weak	1.90	12 2 0
16	Very weak	1.83	12 4 2
17	Weak	1.65	13 0 0
18	Very weak	1.48	12 10 0
19	Very very weak	1.43	12 10 4

an identical type of fine structure, i.e., indicates that the atoms are situated in identical positions in the molecule and that the values of the interatomic distances are similar.

SUMMARY

1. In the formation of germanovanadomolybdic heteropolyacid, isomorphous replacement of molybdenum by vanadium in the heteropoly anion takes place.

2. The composition of germanovanadomolybdic heteropolyacid should be expressed by the formula $H_8[GeMo_{10}V_2O_{40}]$, and not $H_8[GeMo_{10}V_2O_{39}]$; as proposed by Ivanov-Emin.

3. Germanomolybdenum blue is a heteropoly compound isostructural with the unreduced yellow form and contains several ions of lower valency molybdenum in the molecule.

4. No breakdown of the heteropoly anion takes place in the formation of molybdenum blue in the presence of phosphorus, arsenic, silicon, germanium and other metals.

5. It is quite obvious that the quantitative determination of different elements in the form of heteropoly blues requires preliminary setting-up of the conditions (mainly hydrogen ion concentration) for quantitative formation of the unreduced heteropolyacid and its subsequent reduction in as mild reducing conditions as possible, without breakdown of the heteropoly anion.

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*In Russian.

COMPLEX COMPOUNDS OF TIN. IV.

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The present communication is a continuation of a series of works [1-3] on the study of mixed complex compounds of tin halides. The results are given of a physicochemical analysis of the systems

$SnCl_4 \cdot 2C_6H_5COOH—C_6H_5NO_2$, $SnCl_4 \cdot 2C_6N_5COOH—CCl_3COOH$ and
$SnCl_4 \cdot 2CH_3COOH—C_6H_5NO_2$.

EXPERIMENTAL

Nitrobenzene, dried over $CaCl_2$, was purified by repeated distillation and fractional freezing-out. The fraction selected (m.p. 5.7°) was distilled (b.p. 203° at 701 mm pressure) and sealed into ampoules. The complex acid $SnCl_4 \cdot 2C_6H_5COOH$ was prepared by mixing exactly stoichiometric quantities of stannic chloride and benzoic acid in benzene. The crystals of the compound were separated from the mother liquor on a glass filter, washed carefully with benzene and then dried in vacuo over P_2O_5; m.p. 96°. The preparation of the remaining specimens and the method of working have been described earlier [1, 2].

TABLE 1

CCl_3COOH concentration		Viscosity (in poises)			Density (g/cm³)		
wt. %	mole %	60°	80°	100°	60°	80°	100°
0.00	0.00	0.804	0.226	0.0985	—	1.5980	1.5625
5.94	16.27	—	—	0.0626	—	—	—
9.89	25.31	—	0.159	0.0658	—	—	—
12.41	30.45	—	0.105	0.0475	—	1.5487	1.5120
26.71	52.96	—	0.0436	0.0272	—	1.5483	1.5125
47.83	73.91	0.0546	0.0301	0.0192	1.5759	1.5437	1.5106
54.90	79.00	—	0.0272	0.0195	1.5732	1.5405	1.5081
76.22	90.83	0.0451	0.0273	0.0183	1.5767	1.5483	1.5195
100.00	100.00	0.0405	0.0260	0.0191	1.6049	1.5771	1.5475

1. The system $SnCl_4 \cdot 2C_6H_5COOH - CCl_3COOH$ was studied from the viscosity and density at 60, 80 and 100° and the electrical conductivity at 100°.

The results of the measurements are given in Tables 1 and 2. The property-composition diagrams are shown in Figure 1.

The viscosity isotherms are curves convex towards the composition axis and give no indication of reaction between the components. The relationship between the logarithm of the viscosity and composition is of a more complex character. The isotherms of the logarithm of the viscosity are S-shaped curves and lie below the additive straight line along the entire concentration range. The specific conductivity isotherms are S-shaped curves; on the introduction of a correction for the viscosity, the conductivity isotherms acquire the form of curves convex towards the composition axis. The path of the corrected conductivity curve is that of the electrical conductivity of the complex acid $SnCl_4 \cdot 2C_6H_5COOH$ itself, and is evidence of the absence of acid-base reaction between the

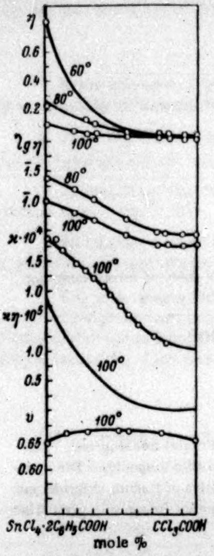

Fig. 1. Viscosity, logarithm of the viscosity, specific conductivity, corrected conductivity and specific volume of the system $SnCl_4 \cdot 2C_6H_5COOH$ – – CCl_3COOH.

TABLE 2

CCl_3COOH concentration (mole %)	$\kappa \cdot 10^{-4}$ (ohm^{-1}·cm^{-1})	CCl_3COOH concentration (mole %)	$\kappa\eta \cdot 10^{-5}$ (ohm^{-1}·cm^{-1})
0.00	1.89	0	1.86
4.79	1.89	10	1.30
9.93	1.67	20	0.864
18.89	1.45	30	0.600
24.73	1.35	40	0.372
30.48	1.20	50	0.204
36.82	1.06	60	0.104
42.23	0.901	70	0.0550
48.27	0.745	80	0.0290
54.20	0.594	90	0.00486
60.82	0.400		
72.20	0.246		
79.31	0.141		

components. It can be seen from an examination of Figure 1 that mixing of the components is accompanied by a considerable expansion.

2. The system $SnCl_4 \cdot 2C_6H_5COOH - C_6H_5NO_2$ was studied from the electrical conductivity, viscosity and density at 60, 80 and 100°, and also by the thermal analysis method. The results of the measurements are given in Tables 3-5. The property-composition diagrams are shown in Figure 2.

The viscosity isotherms at all temperatures are curves convex towards the composition axis, and their shape gives no indication of reaction between the components. Taking consideration of the fact that log η is an additive property [4] we plotted the relationship between viscosity and composition using semilogarithmic coordinates. The isotherms of the logarithm of the viscosity are curves concave towards the composition axis; in our opinion, such a shape for the curves is evidence of reaction in the system [2].

TABLE 3

$C_6H_5NO_2$ concentration		Viscosity (in poises)			Density (g/cm^3)		
wt. %	mole %	60°	80°	100°	60°	80°	100°
0.00	0.00	0.804	0.226	0.0985	—	1.5980	1.5625
2.50	9.49	—	—	0.0840	—	—	1.5395
5.82	20.22	—	0.152	0.0678	—	—	—
9.90	31.02	—	0.120	0.0512	—	—	1.4883
14.21	40.43	0.237	0.0900	0.0462	1.5194	1.4967	1.4698
19.61	50.00	0.143	0.0639	0.0352	1.4950	1.4738	1.4458
29.25	62.89	0.0814	0.0405	0.0281	1.4550	1.4282	1.4040
35.50	69.30	0.0553	0.0320	0.0210	1.4216	1.3991	1.3724
49.48	80.06	0.0334	0.0220	0.0158	1.3589	1.3357	1.3114
65.53	88.63	0.0210	0.0135	—	1.3020	1.2670	1.2425
100.00	100.00	0.0114	0.00873	—	1.1658	1.1445	1.1349

TABLE 4

$C_6H_5NO_2$ concentration (mole %)	$\varkappa \cdot 10^{-4}$ (ohm^{-1} · cm^{-1})			$C_6H_5NO_2$ concentration (mole %)	$\varkappa\eta \cdot 10^{-4}$ (ohm^{-1} · cm^{-1})	
	60°	80°	100°		80°	100°
0.00	—	0.763	1.89	0	1.73	1.86
14.82	—	0.987	—	10	1.43	1.62
20.22	—	0.981	2.64	20	1.52	1.76
30.23	—	1.63	—	30	1.75	1.90
31.02	—	—	3.88	40	1.91	2.14
37.49	—	2.00	—	50	1.93	2.15
40.43	1.11	—	4.99	60	2.20	1.95
43.86	—	2.30	—	70	1.84	1.41
50.00	1.57	3.02	6.10	80	1.23	0.88
55.86	—	3.67	—	90	0.74	0.46
59.12	—	4.22	—			
62.73	—	4.45	—			
62.89	2.41	4.47	7.23			
69.30	3.10	5.63	7.09			
73.10	—	5.71	—			
80.06	4.25	5.82	6.90			
88.63	4.57	4.83	5.86			

The specific conductivity isotherms are curves (Figure 2) passing through a maximum. With increase in temperature the maximum is shifted towards the complex acid $SnCl_4 \cdot 2C_6H_5COOH$.

As nitrobenzene is added to $SnCl_4 \cdot 2C_6H_5COOH$, the corrected conductivity falls slightly at first, passes through a minimum value at ~10 mole % nitrobenzene, and then increases, reaching a maximum value at 50 mole %, after which it falls towards the nonconducting nitrobenzene.

TABLE 5

$C_6H_5NO_2$ concentration (mole %)	Temperature of start of crystallization	Crystallization temperature of eutectic
0.00	96.0°	–
19.11	89.0	–5.0°
29.07	85.5	–4.1
37.73	80.0	–
50.65	73.0	–
61.15	61.0	–
72.22	46.0	–
79.65	30.5	–4.1
87.73	11.5	–4.5
91.44	2.0	–
93.30	0.0	–
100.00	5.7	–

The electrical conductivity of the system $SnCl_4 \cdot 2C_6H_5COOH - C_6H_5NO_2$ is made up of the electrical conductivity arising as a result of acid-base reaction and the electrical conductivity of

$$SnCl_4 \cdot 2C_6H_5COOH$$

itself. We have attempted to separate that part of the electrical conductivity arising as a result of acid-base reaction. For this the value of the conductivity of the system

$$SnCl_4 \cdot 2C_6H_5COOH - CCl_3COOH$$

(Figure 2, Curve II) was subtracted from the value of the conductivity of the system $SnCl_4 \cdot 2C_6H_5COOH - C_6H_5NO_2$ (Figure 2, Curve I). The difference in the values of the conductivities of these systems is represented by Curve III. It can be seen from an examination of the shape of these curves that the highest value of the corrected conductivity corresponds to an equimolecular composition. Since the corrected conductivity is proportional to the ion concentration, it follows that the maximum on Curve III indicates the formation of a compound $SnCl_4 \cdot 2C_6H_5COOH \cdot C_6H_5NO_2$. The fusion diagram for the system consists of two curves intersecting in a eutectic point (93 mole % $C_6H_5NO_2$, –4.5°). The fusion diagram gives no indication of interaction in the system. No noticeable change in volume takes place when the components are mixed.

We therefore conclude from the results of the viscosity and electrical conductivity measurements that a mixed complex compound $SnCl_4 \cdot 2C_6H_5COOH \cdot C_6H_5NO_2$ is formed.

3. The system $SnCl_4 \cdot 2CH_3COOH - C_6H_5NO_2$ was studied from the electrical conductivity, viscosity and

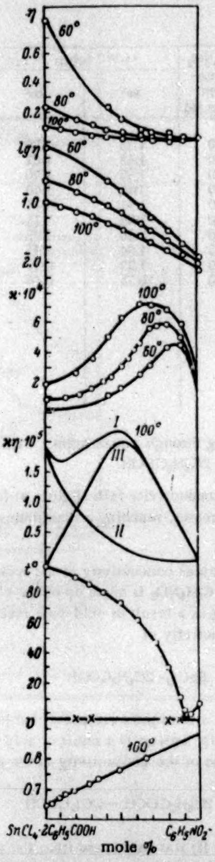

Fig. 2. Viscosity, logarithm of the viscosity, specific conductivity, corrected conductivity, specific volume and fusibility of the system $SnCl_4 \cdot 2C_6H_5COOH - C_6H_5NO_2$.

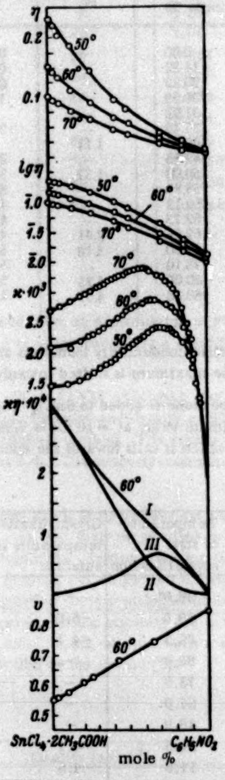

Fig. 3. Viscosity, logarithm of the viscosity, specific conductivity, corrected conductivity and specific volume of the system $SnCl_4 \cdot 2CH_3COOH - C_6H_5NO_2$.

density at 50, 60 and 70°. The results of the measurements are given in Tables 6 and 7 and in Figure 3.

It is seen from an examination of Figure 3 that the viscosity isotherms are convex, and the isotherms of the logarithm of the viscosity concave, towards the composition axis. The shape of the curves showing the relationship between the logarithms of the viscosity and the composition indicates reaction between the components.

The specific conductivity isotherms pass through a maximum, which is shifted towards the complex acid with increase in temperature. The corrected conductivity falls from the conductivity of the complex acid itself towards the nitrobenzene. The corrected conductivity isotherms are curves with a point of inflection. As in the

TABLE 6

$C_6H_5NO_2$ concentration		Viscosity (in poises)			Density (g/cm^3)		
wt. %	mole %	50°	60°	70°	50°	60°	70°
0.00	0.00	0.230	0.149	0.0993	1.8136	1.7949	1.7739
0.76	2.27	0.218	0.140	0.0949	1.8035	1.7874	1.7689
1.75	5.20	0.202	0.132	0.0894	1.7957	1.7742	1.7615
2.59	13.16	0.181	0.115	0.0778	1.7662	1.7514	1.7328
9.78	25.09	0.144	0.0910	0.0638	1.7337	1.7174	1.7023
18.77	41.66	0.0956	0.0662	0.0475	1.6529	1.6367	1.6216
24.59	50.20	0.0758	0.0535	0.0389	1.6108	1.5939	1.5744
43.72	70.61	0.0405	0.0309	0.0237	1.4715	1.4603	1.4466
64.91	85.12	0.0236	0.0188	0.0155	1.3446	1.3329	1.3225
100.00	100.00	0.0129	0.0114	0.0101	1.1750	1.1658	1.1540

TABLE 7

$C_6H_5NO_2$ concentration (mole %)	$\varkappa \cdot 10^{-4}$ (ohm^{-1} · cm^{-1}), at 50°	$C_6H_5NO_2$ concentration (mole %)	$\varkappa \cdot 10^{-4}$ (ohm^{-1} · cm^{-1}), at 60°	$C_6H_5NO_2$ concentration (mole %)	$\varkappa \cdot 10^{-4}$ (ohm^{-1} · cm^{-1}), at 70°	$C_6H_5NO_2$ concentration (mole%)	$\varkappa\eta \cdot 10^{-4}$ (ohm^{-1} · cm^{-1}) 50°	60°	70°
0.00	14.5	0.00	21.1	0.00	27.1	0	3.39	3.14	2.69
10.44	14.5	12.45	20.9	5.43	27.6	10	2.85	2.65	2.33
18.68	15.7	18.53	22.0	10.74	28.5	20	2.46	2.30	2.07
23.06	16.4	22.63	22.6	18.43	29.6	30	2.15	1.97	1.81
27.37	16.9	26.33	22.9	20.54	29.8	40	1.85	1.73	1.57
30.85	17.6	30.93	23.6	24.35	30.0	50	1.59	1.42	1.32
35.43	18.1	32.68	24.1	28.34	30.9	60	1.30	1.21	1.05
38.24	18.9	37.67	24.9	31.84	31.3	70	1.01	0.92	0.82
40.83	19.0	42.76	25.8	32.71	31.5	80	0.70	0.65	0.57
43.21	19.5	45.96	26.3	37.10	31.8	90	0.39	0.35	0.30
46.42	20.5	47.43	27.0	38.64	31.9				
50.26	21.0	50.56	27.5	39.18	32.3				
52.95	21.5	53.73	27.9	41.65	32.6				
55.25	22.0	59.30	28.3	41.73	32.3				
56.89	22.4	61.84	28.5	43.45	32.8				
60.00	22.8	65.11	28.9	46.54	32.9				
62.21	23.4	66.59	28.9	47.93	33.3				
65.43	24.0	74.33	28.0	48.20	33.3				
67.79	24.1	78.27	27.8	50.92	33.6				
69.29	24.1	81.91	27.0	52.09	33.6				
70.65	24.1	86.29	24.5	56.15	33.6				
72.12	24.2	88.24	22.9	58.85	33.6				
73.46	24.0	90.79	19.7	60.35	33.4				
74.80	24.0	93.65	15.6	63.27	33.5				
75.86	23.9			68.78	32.9				
77.22	23.8			69.36	32.6				
78.71	23.5			70.55	32.3				
81.19	23.1			73.64	31.8				
85.16	21.8			76.30	31.2				
89.19	19.3			78.24	30.6				
91.86	16.5			81.64	29.8				
95.12	12.1			83.88	27.3				
				85.85	24.4				
				87.63	23.4				
				91.19	18.9				

previous system, we excluded the conductivity of the $SnCl_4 \cdot 2CH_3COOH$ itself, whose dependence on the concentration is expressed by Curve II (Figure 3), and obtained Curve III, passing through a maximum in the region of 67 mole % nitrobenzene, which corresponds to the compound $SnCl_4 \cdot 2CH_3COOH \cdot 2C_6H_5NO_2$. Curve I in Figure 3 refers to the system $SnCl_4 \cdot 2CH_3COOH - C_6H_5NO_2$, Curve II refers to the system $SnCl_4 \cdot 2CH_3COOH - CCl_3COOH$ [2]. No change in volume takes place when the components are mixed. It may therefore be concluded from the measurements of the viscosity and electrical conductivity of the system $SnCl_4 \cdot 2CH_3COOH - C_6H_5NO_2$ that the mixed complex compound $SnCl_4 \cdot 2CH_3COOH \cdot 2C_6H_5NO_2$ is formed.

SUMMARY

1. A study has been made of the viscosity and density at 60, 80 and 100°, and of the electrical conductivity at 100°, of the system $SnCl_4 \cdot 2C_6H_5COOH - CCl_3COOH$. The absence of an acid-base reaction between the components has been established.

2. A study has been made of the viscosity, density and electrical conductivity at 60, 80 and 100°, and of the fusibility, of the system $SnCl_4 \cdot 2C_6H_5COOH - C_6H_5NO_2$. It has been established that the components react with the formation of the complex compound $SnCl_4 \cdot 2C_6H_5COOH \cdot C_6H_5NO_2$.

3. A study has been made of the viscosity, density and electrical conductivity of the system $SnCl_4 \cdot 2CH_3COOH - C_6H_5NO_2$ at 50, 60 and 70°. The existence of a mixed complex compound $SnCl_4 \cdot 2CH_3COOH \cdot 2C_6H_5NO_2$ has been inferred.

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ENTHALPIES OF FORMATION OF BINARY COMPOUNDS OF THE ELEMENTS OF THE MAIN SUBGROUP OF GROUP V

THE PHENOMENON OF SECONDARY PERIODICITY

S.M. Ariya, M.F. Morozova and S.A. Shchukarev

In 1915 E.V. Biron [1] pointed out the existence of the phenomenon of secondary periodicity, i.e., the irregular change in the properties of the elements of the main subgroups of the periodic system on moving within them in the direction of increasing atomic number. This work, which has a very great significance for the understanding of the periodic law, has for a long time failed to attract the attention it deserves, although its importance in applied science is also extremely great. The change in many of the properties of the chemical elements probably obeys the law of secondary periodicity, but we shall examine here only the secondary periodicity of the enthalpies of formation, taking the elements of the main subgroup of Group V as examples.

As far as the heats of formation of binary compounds are concerned, the phenomenon of secondary periodicity is shown in the fact that on going from a compound of an element in the second period to the compound of the element in the third period the heat of formation increases, on going to the compound in the fifth (fourth) period it falls, to the compound of the element in the seventh (fifth) period it increases and on to the compound in the ninth (sixth) period it again falls. Sometimes, in the case of a less well-defined manifestation of secondary periodicity, the sections showing the increases and decreases on the heat of formation-atomic number curve are replaced by sections showing a steeper or less steep increase or of slow and rapid decrease. The irregular, zig-zag change in certain of the properties of the main subgroups was noticed after E.V. Biron by a number of authors, but they were apparently unacquainted with his work. Thus Klemm and Westlinning [2] have pointed out the irregular change in the values of the ionic radii of the main subgroup of Group V, and have related its appearance to the contraction of the atoms which takes place as a result of the filling of the inner d- and f-levels with electrons in certain regions of the periodic system. Hillebrandt [3] has pointed out the irregular change in the heats of-formation of a number of compounds of the elements of the main subgroups of the periodic system and has shown the existence of an antibathic connection between the irregular change in the heats of formation and a similar irregular change in the energies of removal from the atoms of a number of electrons equal to the number of the group.

None of these authors, however, have considered the irregular change in the properties of the elements of the main subgroups as one of their important general properties.

Kh. Balarev [4] also, apparently unaware of E.V. Biron's work, in 1950 again "discovered" the phenomenon of secondary periodicity and quite correctly pointed out its considerable fundamental importance.

S.A. Shchukarev [5-7] has pointed out that the most clearly defined secondary periodicity is shown in the change in ionization potentials (mainly those associated with removal of s-electrons) and has observed that the irregular, secondary-periodic change in the heats of formation is a reflection of this irregular change in one of the most important energy characteristics of the isolated atoms – their ionization potentials. The secondary periodicity of the enthalpies of formation in a number of instances (see below) is shown very clearly, in some cases it is scarcely noticeable; interest has therefore been attached to a closer definition of the limits of occurrence of this important phenomenon. In this connection the Department of Inorganic Chemistry of the Leningrad State University are carrying out systematic thermochemical studies with the aim of accumulating the experimental material necessary for an approach to a deeper understanding of the phenomenon of secondary periodicity.

It seemed expedient to us to begin the discussion with the change in the heats of stepwise aggregation of the atoms of the elements of the main subgroup of Group V. The upper curve in Figure 1 represents the change in the values of the energy of formation of the molecule E_2 from the free atoms. It is readily seen that in this case no secondary periodicity is observed. The bond in the E_2 molecules is formed by unexcited p-electrons and the bonds in these molecules are typically atomic.

We may thus state straight away that there is no secondary periodicity in the change in the heats of formation of compounds containing atomic bonds formed by unexcited electrons.

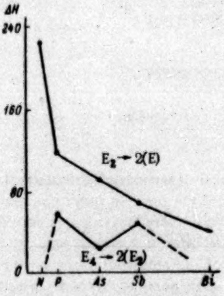

Fig. 1. Heats of dissociation of the molecules E_4 and E_2.

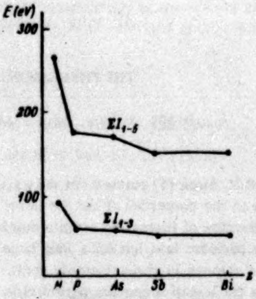

Fig. 2. The change in the third and fifth ionization potentials of the atoms of the elements of the main subgroup of Group V.

The lower curve of Figure 1 gives the change in the heats of dimerization of the molecules E_2. In the case of arsenic, antimony and bismuth (phosphorus, arsenic and antimony) these values are known; in the case of nitrogen and bismuth E_4 molecules are not formed, which gives us grounds for directing the corresponding sections of the curve approximately towards zero ordinate.

The secondary periodicity is here shown exceptionally clearly, and the antibathic relationship to the change in the third and fifth ionization potentials of the elements in question is also clearly seen (Figure 2).

The bonds in the molecules E_4, being bonds between identical atoms, are of course atomic. It appears to us that the reason for the appearance of secondary periodicity at this stage of the aggregation of the atoms N...Bi may be found in the excitation of higher valency states on formation of the molecule E_4, i.e., in the excitation of the s-electrons. Indeed it is difficult to imagine that a mere rearrangement of the same bonds could be responsible for the large thermal effects of the processes $2E_2 \rightarrow E_4$, which are observed in the case of phosphorus, arsenic and antimony. In addition, there is a striking symbathic relationship between the tendency of the elements of the main subgroup of Group V to form E_4 molecules and compounds in which they are in the pentavalent state. In the case of nitrogen and bismuth the pentavalent state is thermodynamically unstable and they do not form E_4 molecules. In the case of phosphorus and antimony the pentavalent state is extremely stable and they form stable E_4 molecules. Arsenic shows a lesser tendency than phosphorus and antimony to form compounds in which it is pentavalent, and the heat of dimerization of the As_2 molecules is less than in the other two elements. The appearance of secondary periodicity under conditions of excitation of the s-electrons for the formation of bonds by them seems to us to be quite natural.

The energies of excitation are of course symbathic with the energies of complete removal from the atoms of the corresponding electrons and consequently an irregularly changing value will figure in the total energy balance of the process of formation of the compound, since the ionization energies of the atoms (especially when removal of the s-electrons is concerned) changes within the main subgroups according to the law of secondary periodicity.

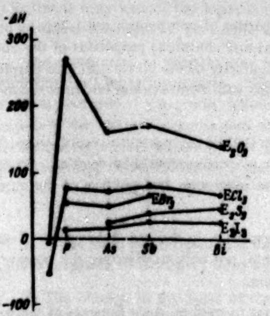

Fig. 3. The change in the enthalpies of formation of the oxides, chlorides, sulfides and iodides of the elements of the main subgroup of Group V.

Our suggestions concerning the excitation of higher valencies in the formation of E_4 molecules should, of course, be further confirmed by a study of the chemical structure of these units. The change in the values of the heats of formation are linked most directly to the ionization energies of the atoms in the case of compounds in which the bonds are ionic, or approach ionic bonds in character, since in this case the ionization energy of the atoms takes the most prominent part in the energy balance of the process of compound formation.

Now Figure 3 indeed shows that the change in the heats of formation of the oxides, chlorides iodides and sulfides, in which the electrons are to some extent removed from the atoms of the elements of the main subgroup of Group V, obeys the law of secondary periodicity.

It is true that here also the secondary periodicity is shown with varying degree of clarity in different series of compounds, which is quite natural, since even in the case of ideally ionic compounds the appropriate sum of the ionization energies of the atoms is not the only factor influencing the magnitude of the heat of formation. Even in the case of a pure ionic bond the magnitude of the heat of formation depends on the radius of the ions and on the heat of atomization of the corresponding simple solids. In real compounds there is added to this the further variation in the degree of deviation of the bond from the purely ionic. The change in the heats of formation of the hydrogen compounds EH_3, both from the simple solids and from the free atoms, does not obey the law of secondary periodicity (Figure 4). We should mention here that all the thermochemical data used in this work, unless otherwise stated, are taken from the latest thermochemical figures [8, 9]. The value of the heat of formation of arsine is taken from the paper [10], as the previously accepted value found by Ogier [11] is erroneous.

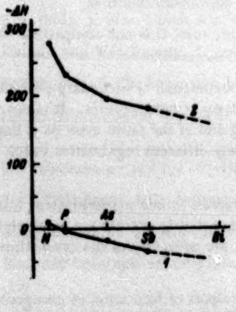

Fig. 4. The change in the enthalpies of formation of the hydrogen compounds of the elements of the main subgroup of Group V: 1) from the simple solids; 2) from the free atoms.

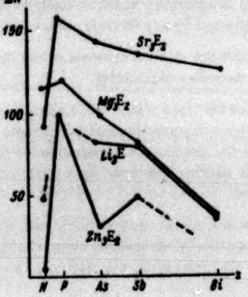

Fig. 5. The change in the enthalpies of formation of the compounds of the elements of the main subgroup of Group V with certain metals.

E.V. Biron discovered the phenomenon of secondary periodicity at a time when the theory of the chemical bond was at an extremely early stage; it was at the time of the now abandoned valency theory of Abegg, which, as is well known, recognized the existence of a normal valency and a contravalency for each element.

Even then, however, E.V. Biron realized that the change in the properties of compounds must depend on the nature of the chemical bond in them. He wrote: ". . . 1) the physical and chemical properties of the compounds formed by the subgroup elements with normal valency obey the regularity of the triads. 2) The physical and chemical properties of the compounds formed by the subgroup elements with contravalencies show secondary periodicity."

Believing that the hydrogen compounds of the elements of Groups IV-VII of the periodic system were formed by normal valencies, E.V. Biron suggested that the change in their properties should be regular. On the other hand, he foresaw that the oxygen compounds of the elements of these subgroups, irrespective of the numerical value of the valency, should obey the law of secondary periodicity.

One cannot but be astonished at the insight with which E.V. Biron was able, in the pre-Bohr epoch of natural science and with the extremely limited experimental material available, not only to discover the phenomenon of secondary periodicity but to point out the limits of its application.

Figure 5 shows the change in the heats of formation of the compounds formed by the elements of the main subgroup of Group V with metals. The values of the heats of formation of the binary magnesium, strontium, lithium and zinc compounds are taken from the latest works [12-21].

There is immediately obvious the contrast between the absence of secondary periodicity in the magnesium and zinc compounds and its well-defined appearance in the zinc compounds, i.e., in the case of divalent metals the secondary periodicity is more clearly defined the less active the metal bound to the elements of the main subgroup of Group V. An analysis of the reasons for such a difference in the change in the enthalpies of formation of the magnesium and strontium compounds on the one hand and of the zinc compounds on the other will be possible after a sufficiently detailed study of the chemical structure of these compounds.

A.F. Kapustinsky [19] has formulated the "thermochemical logarithmic" rule according to which ". . . . . the heats of formation of compounds, relative to one equivalent, are a linear function of the logarithm of the Mendeleev number (atomic number) of the atoms for atoms which are electronically analogous." It should be noted that the thermochemical logarithmic rule is not the only attempt to describe the relationship between the properties of the elements and the place occupied by them in the periodic system, by a mathematical formula. This tendency is apparently fundamentally incorrect: the interrupted, uneven change from one element to another cannot be expressed by any formula, which supposes the existence of a continuous function.

As regards the specific example of the thermochemical logarithmic rule, it is not compatible with the existence of secondary periodicity.

In one of his latest works A.F. Kapustinsky [20] asserts that the phenomenon of secondary periodicity does not contradict the thermochemical logarithmic rule, but, as it were, makes it more precise. It is not clear to us, however, how the change in the enthalpies of formation can be zig-zag and at the same time be a linear function of atomic number. Here we are clearly dealing with two completely different regularities which are quite irreconcilable.

In general it seems strange that it should be thought possible to express in one mathematical formula the change in properties of compounds where changes are taking place (and certainly not always regularly) in the nature of the chemical bond, the effective valency states of the atoms, the geometry of the crystalline structure, etc.

The number of factors which influence the magnitude of the enthalpies of formation of compounds is inexhaustible. The task at the present time is to approach an understanding of them, and not to pick out a formula with two empirical "constants." Such an approach has no theoretical cognitive value; it is even harmful since it may demobilize the research worker by creating the illusion of the existence of some sort of simplicity in what is in reality still a complex and little-understood problem.

The possibility of making practical use of such regularities is also more than doubtful. S.A. Shchukarev's idea concerning the connection between the magnitudes of the enthalpies of formation of binary compounds and the energy characteristics of the atoms forming them, which is accurate in principle, was taken up by V.P. Shishokin [21]. Unfortunately, however, V.P. Shishokin has followed in the search for mathematical formulas relating the enthalpies of formation to the ionization potentials.

For some of the groups of the periodic system he puts forward formulas expressing the enthalpies of formation as linear functions of the logarithm of the equivalent ionization potential; for other groups he expresses them as linear functions of the square root of the ionization potential, etc.

The same critical remarks may be made of these works of V.P. Shishokin as were made concerning the thermochemical logarithmic rule. The enthalpy of formation is a function not only of the magnitude of the ionization energies of the atoms, which only in the case of a few series of compounds completely determines the direction of the change in enthalpies of formation; more often a definite influence is exerted on the enthalpies of formation by factors which are not single factors, and it is therefore incorrect to try to find a formula expressing the enthalpy of formation as a function of the ionization energies of the atoms alone.

SUMMARY

1. It has been established that the change in the heats of formation of the molecules E_2 (E is an element in the main subgroup of Group V) from the free atoms does not obey the rule of secondary periodicity.

2. The change in the heats of formation of the molecules E_4 from the molecules E_2 obeys the law of secondary periodicity, and this may be considered as being explained by the excitation of higher valencies, for which the s-electrons are responsible, in the formation of the E_4 molecules.

3. There is practically no sign of secondary periodicity in the change in the heats of formation of the hydrogen compounds of the elements of the main subgroup of Group V.

4. The change in the heats of formation of the compounds of the elements of the main subgroup of Group V with metals is sometimes regular and sometimes obeys the law of secondary periodicity. In the case of divalent metals the secondary periodicity is more clearly shown the less active the metals combined with the N . . . Bi.

5. The important conditions for the manifestation of secondary periodicity in the change in the heats of formation of binary compounds of the elements of the main subgroup of Group V may be taken to be the excitation of higher valency states and to a greater or lesser extent the ionic character of the chemical bond.

6. It is noted that the thermochemical logarithmic rule is not in accordance with the extensive manifestation of the phenomenon of secondary periodicity and its fundamental significance.

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POLAROGRAPHIC DETERMINATION OF 2,2'-AZOBISISOBUTYRONITRILE, ALIPHATIC AND AROMATIC NITRILES

M.I. Bobrova and A.N. Matveeva

In many studies on the thermal decomposition of 2,2'-azobisisobutyronitrile, 2-azobis-2-methylbutyronitrile, and other aliphatic azonitriles, it has been shown that the amount of nitrogen evolved in the breaking down of an azonitrile is a measure of the rate of this process [1-3].

In some investigations of the thermal decomposition of azonitriles and of the deactivation reactions of the radicals formed, the reaction products have been separated and analyzed [4, 5].

Baun and Mellish [6] employed for this purpose a color reaction between the radicals of the initiating material and α,α'-diphenyl-β-picrylhydrazyl. Ziegler, Deparade and Meye [7] used a color reaction of the free radicals with chloranil.

Bevington [8] studied the thermal decomposition of 2,2'-azobisisobutyronitrile by the method of isotope markers.

A series of investigations has shown that the products of deactivation of the free radicals obtained are mono-, di-, and more complex nitriles.

It was of interest to look into the possibility of using the polarographic method for the investigation of the thermal decomposition of various azodinitriles, and also for the investigation of the kinetics of polymerization and copolymerization with nitriles as the initial monomers.

In the literature very little attention has been paid to the polarography of nitriles. In the work of Bird and Hall [9] acrylonitrile, propionitrile, lactonitrile, and some nitrile derivatives were subjected to reduction at a dropping mercury electrode, but unfortunately the authors did not cite the necessary data on the characteristics of the capillary. Spillane [10] reduced the nitrile of methacrylic acid. In a study by Ogura [11] on electrolytic reduction at a lead electrode, instead of a dropping mercury electrode, the author showed the difficulty of reducing nitriles of the aliphatic series.

EXPERIMENTAL

The objects of our study were 2,2'-azobisisobutyronitrile and the nitriles that are listed with their chief characteristics in Table 1.

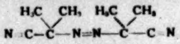
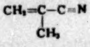
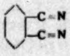
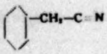
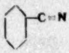
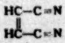
The 2,2'-azobisisobutyronitrile was a commercial product with added stabilizer. By three recrystallizations from hot methyl alcohol which had previously been carefully purified, a product was obtained that melted at 101°.

The nitriles of acetic and methacrylic acids and the dinitriles of fumaric and o-phthalic acids were synthesized by the methods given in References [12-15]. The nitrile of benzoic acid was synthesized by method [16].

All of the nitriles mentioned were synthesized immediately before polarographing and were used in the freshly distilled or recrystallized condition.

Polarographing was carried out with concentrations from 0.5 to 25 millimoles/liter. Aqueous and alcohol-water solutions of the following salts were tried as background electrolytes: $(CH_3)_4NI$, $(C_2H_5)_4NCl$, $(C_2H_5)_4NI$, $(C_4H_9)_4NI$, $C_3H_4(OH)(COOLi)_3$, LiCl.

TABLE 1

No.	Name and formula of nitriles	Boiling point	n_D^{20}
1	2,2'-Azobisisobutyronitrile (azodinitrile of isobutyric acid) 	101° (m.p.)	—
2	Acetonitrile $CH_3{-}C{\equiv}N$	60—61	1.3488
3	Adiponitrile $N{\equiv}C{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}C{\equiv}N$	293—294	1.4538
4	Acrylonitrile $CH_2{=}CH{-}C{\equiv}N$	78—79	1.3920
5	Methacrylonitrile  $CH_2{=}\underset{\underset{CH_3}{\vert}}{C}{-}C{\equiv}N$	90—92	1.400
6	Phthalonitrile 	140—142 (m.p.)	
7	Phenylacetonitrile 	231	1.5442
8	Benzonitrile 	189—190.5	1.5287
9	Fumaronitrile  $\begin{array}{l}HC{-}C{\equiv}N\\ \Vert\\ HC{-}C{\equiv}N\end{array}$	96 (m.p.)	—

Measurements were made on the M-7 polarograph with a mirror galvanometer with a sensitivity of 150 mm/μa, mainly with shunts 1:10 and 1:25. Cylindrical capillary, $t = 3$ sec, $m^{2/3} \cdot t^{1/6} = 1.83$ mg$^{2/3}$ sec$^{-1/2}$ at a potential of 2.1 v referred to a saturated calomel electrode. The height of elevation of the bulb with the mercury provided for possible decrease in the tangential movements [17].

The polarographic measurements were preceded by measurements of the pH of the nitriles and the background electrolytes, and also of solutions of the polarographed nitriles at corresponding concentrations. The pH of the background electrolytes used by us, the nitriles, and the solutions of the nitriles of various concentrations in the background electrolyte varied from 7 to 8.

It should be noted that the pH values before and after polarographing and also upon repeated measurements made after 1, 2, 24 and 48 hours remained unchanged. On this basis we have assumed that the nitriles in the solvents and background electrolytes used were not subject to hydrolysis.

Since the buffer mixtures prevailing in practice for physicochemical measurements do not permit carrying out reduction in the range of strongly negative potentials, we carried out the polarographing of the nitriles in neutral medium. The data for the polarographic investigation of the nitriles are presented in Table 2.

DISCUSSION OF RESULTS

2,2'-Azobisisobutyronitrile is reduced rather easily in various background electrolytes such as aqueous-al-

TABLE 2

No.	Name of nitrile	Background	Reducibility	Concentration of nitrile (mmoles/liter)	$E_{1/2}$ referred to saturated calomel electrode	Constant
1	2,2'-Azobisisobutyronitrile	$(C_4H_9)_4NI$ +50% C_2H_5OH *	Yes	6.0	—1.32	3.39
				8.0	—1.34	3.36
				10.0	—1.33	3.21
				12.0	—1.34	3.40
				14.0	—1.35	3.27
2	Acetonitrile	$(C_2H_5)_4NCl$ $(C_2H_5)_4NI$ $(C_4H_9)_4NI$ $C_3H_4(OH)(COOLi)_3$ LiCl	No	—	—	—
3	Acrylonitrile	LiCl +50% C_2H_5OH	Yes	0.5	—2.34	2.56
				1.0	—2.34	2.68
				1.5	—2.34	2.47
				2.0	—2.36	2.44
				2.5	—2.36	2.50
				3.0	—2.37	2.56
4	Methacrylonitrile	$(C_2H_5)_4$ NI (aqueous solution)	Yes	1.0	—2.22	2.17
				2.0	—2.27	2.05
				3.0	—2.27	1.96
				4.0	—2.30	2.07
				5.0	—2.35	2.02
5	Fumaronitrile	$(C_2H_5)_4$ NI (aqueous solution) 0.2 м.)	Yes	0.855	—1.48	2.32
				1000	—1.50	2.50
				1710	—1.54	2.30
				2565	—1.69	2.48
				3000	—1.71	2.41
				3420	—1.81	2.46
				4275	—1.84	2.44
6	Benzonitrile	$(C_2H_5)_4$ NI $C_3H_4(OH)(COOLi)_3$ LiCl	No	—	—	—
7	Phthalonitrile	$C_3H_4(OH)(COOLi)_3$+ 50% C_2H_5OH	Yes	3.0	—1.92	1.20
				6.0	—1.97	1.20
				9.0	—1.97	1.01
				10.0	—1.99	1.16
				12.0	—1.94	1.03
				15.0	—1.99	1.10
				20.0	—2.02	0.9
				25.0	—2.04	0.92
8	Phenylacetonitrile	Same as in No. 2.	No	—	—	—
9	Adiponitrile	Same	No	—	—	—

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*2,2'-Azobisisobutyronitrile was reduced in alcohol-water solutions of $(C_2H_5)_4NCl$ and $(C_2H_5)_4NI$.

coholic solutions of $(C_4H_9)_4NI$, $(C_2H_5)_4NCl$ and $(CH_3)_4NI$, as indicated by the comparatively small value of the cathode half-wave potential. The magnitude of the diffusion current is proportional to the concentration and is considerably higher than for the nitriles polarographed by us (Figure 1).* The nitriles behave differently when polarographed. Only those nitriles are reduced that have double bonds in the molecule that are conjugated with the bond in the CN group. Thus, for example, acetonitrile and adiponitrile are not reduced, but acrylonitrile, methacrylonitrile, and fumaronitrile are reduced. In exactly the same way phenylacetonitrile and benzonitrile are not reduced at the dropping mercury electrode, although in the latter the nitrile bond is conjugated with a double bond of the benzene ring. Phthalonitrile, in which there is a conjugated double bond, is subject to reduction. There are analogous examples in the polarographing of various classes of unsaturated compounds [18, 19].

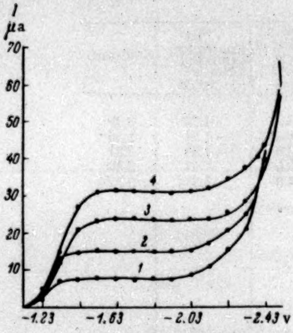

Fig. 1. Polarograms for 2,2'-azobisisobutyronitrile [carrier – 0.05 M $(C_4H_9)_4NI$ in 50% C_2H_5OH]. Concentration (millimoles/liter): 1) 2; 2) 4; 3) 6; 4) 8.

Acrylonitrile, methacrylonitrile and the dinitriles of fumaric and phthalic acids are reduced under considerably more severe conditions than 2,2'-azobisisobutyronitrile, as indicated by their considerably more negative half-wave potentials.

The polarographic behavior of the fumaronitrile differs considerably from the other nitriles in that less severe conditions are required for its reduction at the dropping mercury electrode (Figure 2).

Furthermore, phthalonitrile follows in ease of reduction, the value of its diffusion current constant being definitely different from those of the other nitriles (Figure 3).

The analysis of the electronic structures of 2,2'-azobisisobutyronitrile and of the nitriles previously listed and the polarographic data permits us to suggest that reduction of 2,2'-bisisobutyronitrile at the dropping mercury electrode occurs at the azo group, but in the case of acrylonitrile, methacrylonitrile and fumaronitrile it takes place at the site of the double bond. Only in phthalonitrile does reduction take place at the nitrile group.

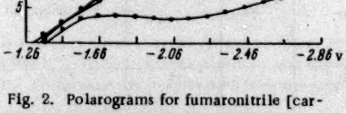

Fig. 2. Polarograms for fumaronitrile [carrier – aqueous solution of $(C_2H_5)_4NI$]. Concentration (millimoles/liter): 1) 0.855; 2) 1.710; 3) 2.565; 4) 3.420; 5) 4.275.

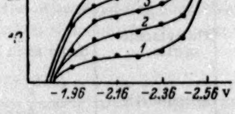

Fig. 3. Polarograms for phthalonitrile [carrier – 0.2 M $C_3H_4(OH)(COOLi)_3$ in 50% C_2H_5OH]. Concentration (millimoles/liter): 1) 3; 2) 6; 3) 9; 4) 12; 5) 15.

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*In Figures 1, 2 and 3 the values given for the potentials are referred to a saturated calomel electrode.

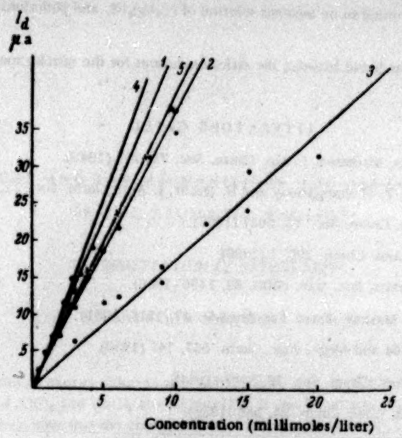

Fig. 4. Relationship of the magnitude of the diffusion current to concentration (calibration lines): 1) fumaronitrile; 2) methacrylonitrile; 3) phthalonitrile; 4) acrylonitrile; 5) 2,2'-azobisisobutyronitrile.

The magnitude of the diffusion current in the reduction of the nitriles was directly proportional to the concentration, as indicated by the straight calibration lines (Figure 4).

The half-wave potentials were determined in two ways – graphically on the basis that the quantity $\log \frac{i}{i_d - i}$ equals zero, and also from the polarograms. The data obtained in the two ways agree.

The half-wave potentials for 2,2'-azobisisobutyronitrile, acrylonitrile, methacrylonitrile, and phthalonitrile showed only a negligible change on going from one concentration to another. Fumaronitrile was an exception to this.

The consumption of electrons per mole of nitriles reduced, determined from the wave relation, was expressed as fractions from 0.22 to 0.6, but in the case of acrylonitrile on the basis of the Ilkovich equation it was 1.17.

The graphical expression of the relation of $\log \frac{i}{i_d - i}$ to the potential of the dropping mercury electrode (referred to a saturated calomel electrode), constructed from the polarograms of the nitriles investigated, yields straight lines.

SUMMARY

1. The possibility has been established of the polarographic reduction of 2,2'-azobisisobutyronitrile and the conditions have been determined.

2. In the instance of acetonitrile, adiponitrile, phenylacetonitrile and benzonitrile, it has been found that the aliphatic nitriles that do not contain a double bond conjugated with the nitrile group are not reduced. Also aromatic nitriles are not reduced, whether or not the nitrile bond is conjugated with a double bond of the ring. Phthalonitrile, however, is reduced.

3. Acrylonitrile was polarographically determined in an alcohol-water solution of LiCl, methacrylonitrile

and fumaronitrile were determined in an aqueous solution of $(C_2H_5)_4NI$, and phthalonitrile in an alcohol-water solution of lithium citrate.

A linear relationship was found between the diffusion current for the nitriles mentioned and their concentrations.

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RADICAL AND ION MECHANISM OF THE ALKYLATION OF THE AROMATIC NUCLEUS

V. BENZYLATION OF NAPHTHALENE

I.P. Tsukervanik and G.S. Semeshko

The first condensations of benzyl chloride with naphthalene were carried out in the presence of zinc dust [1]. Vincent and Roux used $AlCl_3$ and $ZnCl_2$ as catalysts [2]. It was found that with $AlCl_3$ at 80° α-benzylnaphthalene was formed; the β-isomer was the chief product of this reaction at 160°. The authors noted that in reactions with $AlCl_3$ appreciable amounts of dinaphthyl always accumulated. Dziewonski [3] reinvestigated the benzylation of naphthalene with the aid of $ZnCl_2$ and showed that various dibenzylnaphthalenes always were formed along with α-benzylnaphthalene. Bogussky [4] obtained similar results with aluminum powder. The benzylation of naphthalene with P_2O_5 also has been described [5, 6]. In condensations of naphthalene with benzyl alcohol [7] and propylbenzyl ether [8], complexes of BF_3 have been employed as catalysts. Scharma and Dutt [9], investigating the catalytic activity of various metals, demonstrated the possibility of using titanium for the synthesis of benzylnaphthalene.

Nenitzescu [10] made the important observation that the reaction in question could be brought about thermally without catalysts; in this way he obtained α-benzylnaphthalene.

Recently Buu-Hoi [11] described the benzylation of methylnaphthalene and a series of polynuclear compounds in the presence of small amounts of $ZnCl_2$. On the basis of the conformance of the orientation of the benzyl group in the products with computations by the method of molecular orbits, the author considered these as radical reactions.

It must be noted that in the publications indicated there is considerable divergence in the constants of the benzylnaphthalenes. Apparently, mixtures of isomers are obtained as a result of the condensations.

Japanese chemists [12] have studied especially the orientation of the benzyl group in relation to the catalyst and the reaction temperature. They have shown by the infrared spectroscopic method that with P_2O_5 (at 180-200°), $ZnCl_2$ (at 80°), $FeCl_3$ (at 80°), and $AlCl_3$ (at 1-30°), predominantly α-benzylnaphthalene is formed (70-80% of the total products). Only in reactions with $AlCl_3$ at 65-70° was β-benzylnaphthalene the chief product (81%).

We have studied the condensation of benzyl chloride with naphthalene in the presence of copper, which has been shown, as demonstrated by one of us [13], to be a good catalyst for the benzylation of the aromatic nucleus. For purposes of comparison, we also repeated the condensations with $ZnCl_2$ and $AlCl_3$ and the thermal condensation. Benzylation of naphthalene without a catalyst went very easily when the mixture of reactants was heated to 170-220° in a flask with a reflux condenser. With a 3-fold molar excess of naphthalene the yield of benzylnaphthalene amounted to 60% of theoretical. Experiments with equimolar quantities of the reactants gave smaller yields (17%) as a result of marked resinification and accumulation of oily fractions that contained dibenzylnaphthalene.

The principal product of the thermal condensations was α-benzylnaphthalene. By fractional crystallization we succeeded in isolating very little β-isomer. It was observed that thermal benzylation proceeds partially in the process of distillation of the mixture of reactants after catalytic reactions carried out at low temperatures (80-90°). This leads to some increase in the yields of benzylnaphthalene.

There is every reason to think that the above-mentioned, previous data pertain in considerable degree to thermal rather than to catalytic reactions, as the authors supposed (for example, with P_2O_5 at 180-200° [12], and with $ZnCl_2$ at 150° [2]).

Our condensations with $ZnCl_2$ (0.3-0.5 gram-mole to 1 gram-mole of $C_6H_5CH_2Cl$) were carried out at 80-90°. Mono- and dibenzylnaphthalenes were obtained in yields of 40 and 5-10% respectively. Condensations at 130-150° have higher yields of benzylnaphthalene (50%) as a result of thermal reaction. In these experiments we obtained almost wholly the α-isomer, but upon fractional crystallization of it we were able to detect a little β-benzylnaphthalene.

In a series of experiments with freshly reduced copper and "copper-bronze" powder, it was ascertained that the reactions went at 80-90°. It was shown to be sufficient to use 0.08 gram-atom of copper. Best results were obtained with a 2-fold molar excess of naphthalene.

As a result of the condensations about 30% of the copper taken was converted to Cu_2Cl_2. In special experiments it was shown that cuprous chloride itself did not catalyze the benzylation of naphthalene under the conditions in question. We found that with a copper catalyst α-benzylnaphthalene (up to 60%) and a little dibenzylnaphthalene were obtained. We were unable to detect β-benzylnaphthalene in the products of the condensations.

Reactions were also carried out in the presence of $AlCl_3$. The amount of $AlCl_3$ varied within the limits 0.1-0.2 gram-mole to 1 gram-mole of benzyl chloride. An appreciable yield (25%) of benzylnaphthalene was obtained only at 75-85°. In the other cases, either the reaction went only very slightly (at 15-25°) or the material was completely resinified (at 160°). The product of condensation in the presence of $AlCl_3$ at 75-85° was β-benzylnaphthalene. We did not succeed in isolating the α-isomer by crystallization.

Comparison of the results of the benzylation of naphthalene carried out under different conditions shows that the α-isomer is predominantly obtained in those cases where it can be assumed that the reaction mechanism is not ionic. However, no dibenzyl or dinaphthyl at all was produced either in thermal condensations or in the presence of copper. Apparently the benzylation of naphthalene proceeds through a reaction complex in which redistribution of the bonds occurs as a result of homolytic rupture. The course of these reactions is evidently determined by the great lability of the α-hydrogens of naphthalene.

EXPERIMENTAL

Thermal benzylation. 20 g (0.16 mole) of naphthalene and 6 g (0.05 mole) of benzyl chloride were heated in a flask with a reflux condenser for 6 hours at 180-220° until the strong evolution of HCl ceased. 11.4 g of naphthalene was distilled off from the reaction mixture (at 230-270°). The residue was distilled in vacuo. The fraction distilling at 160-170° at 3 mm crystallized completely. 6.2 g (60%) of α-benzylnaphthalene with m.p. 58° was obtained. About 0.05 g of β-benzylnaphthalene was isolated by fractional recrystallization from alcohol. In addition, 2 g of a greenish-yellow fluorescent oil and 3.4 g of solid resin were obtained. From the oil 1 g (14%) of dibenzylnaphthalene was isolated by repeated vacuum distillation.

Benzylation in the presence of $ZnCl_2$. A mixture of 25 g (0.2 mole) of naphthalene, 16.5 g (0.13 mole) of benzyl chloride, and 8.5 g (0.062 mole) of $ZnCl_2$ was heated for 8 hours on a boiling water bath (80-90°). 11.9 g of naphthalene, 11.3 g (40%) of α-benzylnaphthalene, 0.04 g of β-benzylnaphthalene, 7.8 g of a fluorescent oil with b.p. 250-270° at 3 mm, and 4.3 g of solid resin were obtained. From the oil 4 g (20%) of dibenzylnaphthalene was obtained. The same reaction carried out at 150° for 2 hours yielded 12.7 g (49%) of α-benzylnaphthalene.

Benzylation in the presence of copper. Either copper freshly reduced from copper sulfate with zinc dust, or "copper bronze" powder (Kahlbaum) was used. Both preparations proved to be equally active. 28 g (0.22 mole) of naphthalene, 13 g (0.1 mole) of benzyl chloride, and 0.5 g of copper were heated for 2 hours on a boiling water bath.

18.7 g of naphthalene, 13 g (60%) of α-benzylnaphthalene, 2 g (13%) of dibenzylnaphthalene, and 1.5 g of an oily residue were separated.

In a case where the crude reaction mixture was treated with steam to remove the unreacted benzyl chloride, the yield of α-benzylnaphthalene was 55%.

Benzylation in the presence of $AlCl_3$. To a mixture of 20.8 g (0.16 mole) of naphthalene and 9.5 g (0.075 mole) of benzyl chloride, heated to 70°, was added 0.8 g (0.006 mole) of $AlCl_3$ in small portions. The reaction was carried on for 8 minutes at 70-80°. The mixture was treated with boiling water and extracted with benzene. After drying, removal of the benzene, and fractionation, the following products were obtained: 10 g of naphthalene, 4 g (25%) of β-benzylnaphthalene, and 0.6 g of tarry residue.

Identification and Analysis of Reaction Products

α-Benzylnaphthalene was isolated by repeated fractional crystallization from alcohol of the crude condensation product. Fine, colorless needles with m.p. 57-58°; b.p. 350° (730 mm); 167° (3 mm). Picrate m.p. 100°. The pure α-benzylnaphthalene (5 g) obtained by us was oxidized with 50% HNO_3 (150 ml) by boiling the mixture for 48 hours. α-Benzoylnaphthalene with m.p. 75° [18] was isolated. This preparation gave no depression in melting point when mixed with the compound synthesized from α-$C_{10}H_7MgBr$ and benzoyl chloride [18].

Upon heating with $AlCl_3$ the α-benzoylnaphthalene obtained by the oxidation of α-benzylnaphthalene, benzanthrone was produced with m.p. 166-169° [19].

β-Benzylnaphthalene was isolated by fractional crystallization of the condensation products from alcohol, in the form of large, regular crystals with m.p. 54.5-55°. Picrate m.p. 93°.

Found %: C 93.49; H 6.51. $C_{17}H_{14}$. Calculated %: C 93.58; H 6.42.

The data in the literature on the melting point of β-benzylnaphthalene are as follows: 35.5° [14, 15], 55.5° [16], 39-40° [9], 54.3-55.3° [17]. In several cases, apparently, the data relate to a mixture of the α- and β-isomers. Such a mixture was also separated out by us, but we were able to obtain the pure compounds by fractional crystallization.

1,8-Dibenzylnaphthalene [20]. By repeated distillation in vacuo of the oily residue from the condensation, a fraction was isolated with b.p. 280-300° at 20 mm in the form of a thick, viscous oil. Upon standing it completely crystallized. Recrystallization from alcohol yielded a little pure 1,8-dibenzylnaphthalene with m.p. 144°.

Found %: C 93.47; H 6.55. $C_{24}H_{20}$. Calculated %: C 93.51; H 6.49.

SUMMARY

1. It has been shown that α-benzylnaphthalene is formed by condensation of naphthalene with benzyl chloride in those cases where a nonionic reaction mechanism is possible. With aluminum chloride as the catalyst, β-benzylnaphthalene is obtained.

2. In the presence of small amounts of copper at 80-90°, 60% of α-benzylnaphthalene was obtained.

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**In Russian.

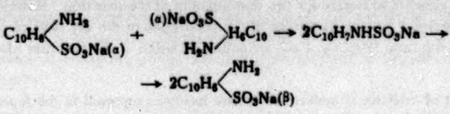
INVESTIGATIONS IN THE NAPHTHALENE SERIES*

XV. THE REARRANGEMENT OF AROMATIC SULFO SALTS; CONVERSION OF THE DRY SALTS OF 2-NAPHTHYLAMINE-1-SULFONIC ACID AND 2-NAPHTHYLSULFAMIC ACID

V. V. Kozlov

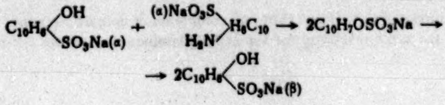
In previous work we have studied the rearrangement of dry salts: of the naphthionate and α-naphthylsulfamate to the salt of 1-naphthylamine-2-sulfonic acid [1] of 1-naphthol-4-sulfonic acid and the salt of the acid sulfate of α-naphthol to the salt of 1-naphthol-2-sulfonic acid [2]; of the salt of 2-naphthol-1-sulfonic acid to the salt of the acid sulfate of β-naphthol, and of the latter to the salt of 2-naphthol-6-sulfonic acid [3].

It has been established that all of these compounds rearrange according to a common scheme with the formation of the following products: a) from the starting salts of naphthylaminesulfonic acids with the sulfo group in the labile α-position – salts of naphthylsulfamic acid, and subsequently salts of naphthylaminesulfonic acids with the sulfo group in the β-position of the naphthalene nucleus



$$C_{10}H_6\left\langle\begin{array}{l}NH_2\\SO_3Na(\alpha)\end{array}\right. + \left.\begin{array}{r}(\alpha)NaO_3S\\H_2N\end{array}\right\rangle H_6C_{10} \longrightarrow 2C_{10}H_7NHSO_3Na \longrightarrow 2C_{10}H_6\left\langle\begin{array}{l}NH_2\\SO_3Na(\beta)\end{array}\right. \qquad (1)$$

b) from the starting salts of naphtholsulfonic acids with the sulfo group in the α-position to salts of naphthol sulfates, and subsequently to salts of new naphtholsulfonic acids with the sulfo group in the β-position of the naphthalene nucleus



$$C_{10}H_6\left\langle\begin{array}{l}OH\\SO_3Na(\alpha)\end{array}\right. + \left.\begin{array}{r}(\alpha)NaO_3S\\H_2N\end{array}\right\rangle H_6C_{10} \longrightarrow 2C_{10}H_7OSO_3Na \longrightarrow 2C_{10}H_6\left\langle\begin{array}{l}OH\\SO_3Na(\beta)\end{array}\right. \qquad (2)$$

In these investigations we showed the incorrectness of some ideas about the course of such rearrangements by way of hydrolysis and resulfonation of the aromatic compound by the pyrosulfate or the bisulfate [4].

Recently E. A. Shilov et al. [5] have employed the radioactive isotope S^{35} to clarify the mechanism of such rearrangements of sulfo salts. They confirmed that in the instances cited above the sulfonate group migrates without interchange with an external sulfate and the rearrangement is an intermolecular reaction. These investigators considered that first the molecule with the amino- or hydroxy-group adds a proton, being converted to a hypothetical intermediate compound of quinoid structure

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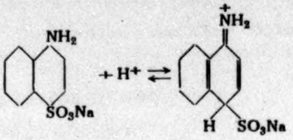
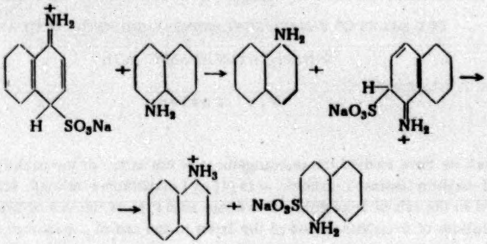
*For XIV communication see J. Gen. Chem. 26, 1775 (1956).



(3)

Such a quinoid compound then sulfonates another molecule of the amine or phenol.

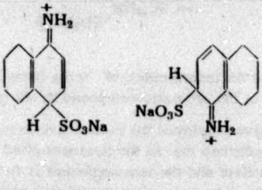


(4)

The hypothesis concerning the formation of a compound of quinoid structure is based on the fact that some rearrangements of sulfo salts are stopped in the presence of sodium carbonate. The authors consider that a certain degree of acidity appears necessary for the development of the reaction. However, in our opinion these assumptions are unconvincing. For the first stage of the conversion of the dry salts of naphthylamine- or naphtholsulfonic acids, a basic medium (Na_2CO_3, CaO, quinoline, dilution of the reaction mass with naphthalene) is not a hindrance.

A positive effect of addition of sodium carbonate has been reported in the rearrangement of naphthionate in naphthalene to the salt of the naphthylsulfamic acid [1], and sodium carbonate and calcium oxide have proved to be harmless in the rearrangement of the 1-naphthol-4-sulfonate [2]. Cessation of the rearrangment of 2-naphthol-1-sulfonate by the action of sodium carbonate [3] is explained solely by the instability of this salt in alkaline medium. Thus, a significant effect of sodium carbonate depends on the properties of the reacting materials, and it is not fitting to accept its action as an explanation for the mechanism of rearrangement.

Starting from the plan of E.A. Shilov [5b], the complexes of quinoid structure, formed by a proton and the sulfo salt, should be of the same reactivity for 1,4-naphthylaminesulfonate and 1,2-naphthylaminesulfonate.

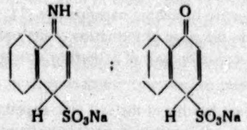


However, it is known that 1,2-naphthylaminesulfonate is not capable of rearranging [1], nor of giving cross reactions with amines and phenols. It must be further noted that it is entirely impossible to represent a structure for a complex of naphtholsulfonates with a proton.

The following facts are important for explaining the migration of sulfonate groups: the absence of rearrangement in the neutral salts of 1-naphthol-4-sulfonic acid [2] and 2-naphthol-1-sulfonic acid [3] where the hydrogen of the hydroxyl in these compounds is replaced by a metal; the absence of rearrangement when the dry sodium salts of 1-methoxynaphthalene-4-sulfonic acid and N-dimethylnaphthionic acid are heated in naphthalene.

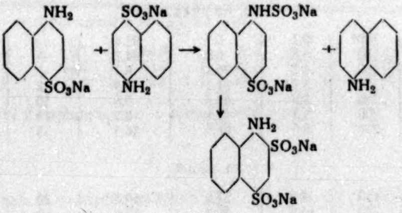
Moreover, for the latter compound (N-dimethylnaphthionic acid) formation of a complex of the sulfonate group with a proton according to the scheme of E.A. Shilov is possible. Thus, ideas about complexes of quinoid structure with a proton and a sulfo salt are hypothetical.

In speaking of the primary act of the rearrangement process, we may rather propose that in the proper media the starting molecules of naphthylamine- or naphtholsulfonates are activated with the formation of quinogen-type structures.



In this case, the absence of rearrangement of salts of N-dimethyl- and 1-methoxynaphthionic acid and of the other compounds mentioned above is fully justified.

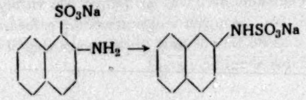
In contrast to E.A. Shilov, we consider that the rearrangement of the dry salts of naphthylaminesulfonic acids (α) and naphtholsulfonic acids (α) proceeds certainly, in either the quinogen or nonquinogen condition, through an intermediate phase of formation of naphthylsulfamates and the corresponding salts of naphthylsulfates. The absence of rearrangement in the free naphthylamine- and naphtholsulfonic acids is explained by the instability of the free naphthylsulfamic acids or naphtholsulfates that are formed. The formation of the compounds of the first phase has been demonstrated in our investigations cited above [1-3]. The appearance in the reaction medium (acid or basic) of naphthylamines or naphthols is a result of partial hydrolysis and breaking down of the starting materials at high temperature. The possibility of the appearance of naphthylamine in the reaction medium in some way (according to E.A. Shilov [5a, 5b] resulfonation of the naphthylaminesulfonic acids) with the formation from the naphthionate of 1-naphthylamine-2,4-disulfonic acid can be explained also from our scheme (5) (incomplete rearrangement)



(5)

As we have shown in the example of the conversion of the salt of 2-naphthol-1-sulfonic acid to the salt of the sulfate of β-naphthol [3], the intermediate stage of rearrangement to the salt of the naphthol sulfate may also be the final result of the rearrangement.

A rearrangement completely analogous to this first stage was discovered by Tobias [6] upon heating the salt of 2-naphthylamine-1-sulfonic acid with its conversion to the salt of β-naphthylsulfamic acid



(6)

The details of this rearrangement are not in the literature. We subjected the dry sodium salt of 2-naphthylamine-1-sulfonic acid to heating with a reflux condenser, with periodic shaking. As diluents we used pure quartz sand and naphthalane. Heating of the salt in both media led first of all to the formation of β-naphthylamine and then, particularly in the sand medium, at high temperature there was observed a deep-seated decomposition of the material with the formation of SO_2, tar, and carbon. The decomposition of the material led to the appearance in the reaction medium of acidity (to litmus). The chief product of the reaction in the naphthalene medium was the sodium salt of β-naphthylsulfamic acid, which was formed even at 100°, and in maximum yield of 81.1% at 170° (Table 1). The rate of conversion of the salt of 2-naphthylamine-1-sulfonic acid to the salt of β-naphthylsulfamic acid is not too great. Only after 4 hours' heating at 150° did the amount of the latter reach 76.1%, and thereafter it increased insignificantly. The conversion of the salt of 2-naphthylamine-1-sulfonic acid proceeded under milder conditions than the conversion of sodium naphthionate [1]. As is known, upon heating the latter it is difficult to hold the rearrangement in the stage of formation of the sodium salt of α-naphthylsulfamic acid, which on the one hand is easily converted to the salt of 1-naphthylamine-2-sulfonic acid, and on the other hand is hydrolyzed to α-naphthylamine.

In contrast to sodium naphthionate, heating of the salt of 2-naphthylamine-1-sulfonic acid is easily held up in the stage of formation of the more stable salt of β-naphthylsulfamic acid. At high temperatures the amount of the salt of β-naphthylsulfamic acid drops as a result of hydrolysis, under the influence of the acid medium, to β-naphthylamine and then its conversion to the salt of 2-naphthylamine-6-sulfonic acid. The content of the latter in the reaction products was comparatively small and only at 218° (boiling naphthalene) and 12 hours' heating did the yield of it amount to 31.9% (Table 2). It is interesting to note that even under these conditions the relatively stable sodium salt of β-naphthylsulfamic acid did not disappear from the reaction mixture (about 8%).

TABLE 1

Rearrangement of the Sodium Salt of 2-Naphthylamine-1-sulfonic Acid (5 g) in Relation to Temperature when Heated in 10 g of Naphthalene or 15 g of Sand for 4 Hours

Experiment No.	Temperature	Yield (in %)				
		β-naphthalene	salt of β-naphthylsulfamic acid	salt of β-naphthylaminesulfonic acid	carbon	total
In naphthalene						
1	100°	0.7	6.7	91.4*	—	98.8
2	130	0.8	6.0	84.3*	—	91.1
3	150	4.2	76.1	8.1	—	88.4
4	170	3.18	81.1	4.9	2	91.2
5	180	3.9	49.2	9.8	10	72.9
6	200	5.3	47.1	9.7	14	76.1
7	218	8.6	66.5	16.5	5	96.6
In sand						
8	150	1.6	17.4	59.8*	10	88.8
9	200	14.5	51.9	19.5	10	95.9
10	220	2.1	38.4	34.9	15	90.4
11	250	7.3	1.4	19.7	35	63.5

*Sodium salt of 2-naphthylamine-1-sulfonic acid.

Heating of the sodium salt of 2-naphthylamine-1-sulfonic acid in sand was associated with strong decomposition of the material and led to the same products as heating in naphthalene, but in different proportions. The amount of the salt of β-naphthylsulfamic acid that was formed was visibly less than in naphthalene and after 4 hours' heating at 200° reached 51.9%. At higher temperatures the percentage of the salt of β-naphthylsulfamic acid in the reaction medium decreased both because of strong charring of the material and as a result of the formation of the salt of 2-naphthylamine-6-sulfonic acid.

The rate of conversion of the starting material to the salt of β-naphthylsulfamic acid in sand was clearly lower; however, at high temperatures in sand the salt of 2-naphthylamine-6-sulfonic acid was formed in large quantities (Tables 1 and 2). The maximum yield of the latter (33.1%) was established at 200° and 8 hours' heating.

In order to explain the nature of all the conversions taking place, we studied the behavior on heating of the dry sodium salt of β-naphthylsulfamic acid. Heating of this salt in naphthalene led to considerable formation of β-naphthylamine and the salt of 2-naphthylamine-6-sulfonic acid, the quantity of which amounted to 32% at 218° (Table 3).

Heating of the salt of β-naphthylsulfamic acid in sand (Table 4) revealed that its conversion to the salt of 2-naphthylamine-6-sulfonic acid proceeds quite rapidly. After 2 hours of heating at 200° there remained in the reaction mass only 1.3% of the starting material with up to 42% of the salt of 2-naphthylamine-6-sulfonic acid. However, the process of heating in sand was accompanied by strong carbonization of the material and the formation of even more β-naphthylamine than in naphthalene. This was the result of the considerable instability of the starting material in acid medium.

TABLE 2

Rearrangement of the Sodium Salt of 2-Naphthylamine-1-Sulfonic Acid (5 g) in Relation to Time

Experiment No.	Time (in hours)	Yield (in %)				
		β-naphthalene	salt of β-naphthylsulfamic acid	salt of β-naphthylaminesulfonic acid	carbon	total
In naphthalene (10 g) at 150°						
1	1	1.7	14.9	76.5 •	—	93.1
2	4	4.2	76.1	8.1	—	88.4
3	6	2.5	79.1	16.1	1.3	99.0
In naphthalene (10 g) at 218°						
4	4	8.6	66.5	16.5	3.5	95.1
5	12	10.9	7.9	31.9	30.0	80.7
In sand (15 g) at 200°						
6	2	5.7	64.9	19.4	5.0	94.9
7	4	14.6	51.9	19.5	10.0	95.9
8	8	11.4	52.0	33.1	3.0	99.5

• Sodium salt of 2-naphthylamine-1-sulfonic acid.

TABLE 3

Conversion of the Salt of β-Naphthylsulfamic Acid in Relation to Temperature (5 g 95.8% salt, 10 g naphthalene, 4 hours)

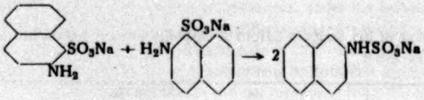
Experiment No.	Temperature	Yield (in %)				
		β-naphthylamine	salt of β-naphthylsulfamic acid	salt of 2-naphthylamine-6-sulfonic acid	carbon	total
1	150°	19.3	65.5	10.1	–	94.9
2	218	33.7	0.6	31.8	20.0	86.1

TABLE 4

Conversion of the Salt of β-Naphthylsulfamic Acid in Relation to Time (5 g 95.8% salt, 15 g sand, 200°)

Experiment No.	Time in hours	Yield (in %)				
		β-naphthylamine	salt of β-naphthylsulfamic acid	salt of 2-naphthylaminesulfonic acid	carbon	total
1	2	21.9	1.3	42.1	30.0	95.3
2	4	38.7	0.7	29.3	30.0	98.8

The conversion of the dry sodium salt of 2-naphthylamine-1-sulfonic acid by heating goes in two stages. In the first stage, which proceeds under relatively mild conditions, the conversion of this material corresponds with the following rearrangement scheme



(7)

TABLE 5

Rearrangement of the Sodium Salts of 2-Naphthylamine-1-sulfonic Acid and β-Naphthylsulfamic Acid in Different Media (5 g salt, 10 g naphthalene, 4 hours, 150°)

Experiment No.	Material	Additive	Yield (in %)			
			salt of β-naphthylsulfamic acid	β-naphthylamine	salt of 2-naphthylaminesulfonic acid	total
1	Sodium salt of 2-naphthylamine-1-sulfonic acid	–	76.1	4.2	8.2*	88.5
2	Same	3 g Na_2CO_3	75.8	6.8	6.9*	89.5
3	Same	3 g $NaHSO_4$	7.0	38.0	39.5	84.5
4	Sodium salt of β-naphthylsulfamic acid	–	65.5	19.3	10.1	94.9
5	Same	3 g Na_2CO_3	78.0	19.5	–	97.5
6	Same	3 g $NaHSO_4$	–	39.0	58.5	97.5

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*Sodium salt of 2-naphthylamine-1-sulfonic acid.

The β-naphthylsulfamate formed was quite stable at low temperatures (up to 150°) and in basic medium. Raising the temperature led to partial combustion of the material and an increase in the acid products (polysulfates), as a result of which hydrolysis of the β-naphthylsulfamate occurred. The β-naphthylamine thus formed was "baked" to 2-naphthylamine-6-sulfonic acid. Lowering the acidity through the effect of liquid phase naphthalene or sodium carbonate (Table 5) limited the conversion of 2-naphthylamine-1-sulfonate to the first stage of the rearrangement to β-naphthylsulfamate. Only a high temperature (218°) and prolonged time of heating (12 hours) ensured that the second stage would gradually proceed in naphthalene. In sand this conversion proceeded much more completely and rapidly because of the conditions which maintained a high concentration of acid agents in close contact with the organic material. Such a process is analogous to the process of "baking" β-naphthylamine with sulfuric acid or polysulfates [7] to 2-naphthylamine-6-sulfonic acid.

Naturally, separate "baking" of β-naphthylamine with the appropriate amount of sulfuric acid creates more favorable conditions for the complete conversion of the β-naphthylamine to 2-naphthylamine-6-sulfonic acid than under our conditions of thermal decomposition, with a small quantity of acid agents. As can be seen from the data (Table 5), an artificial increase in the concentration of bisulfate promotes the conversion of β-naphthylsulfamate to 2-naphthylamine-6-sulfonate. The whole process of conversion of 2-naphthylamine-1-sulfonate and β-naphthylsulfamate to 2-naphthylamine-6-sulfonate is analogous to the conversion described by us of 2-naphthol-1-sulfonate and the salt of β-naphthol sulfate [3].

The process of independent sulfonation occurred also in the experiments of E.A. Shilov [5]. Thus, from his results (Table 1 in [5b]) it follows that a very considerable exchange was observed with the external sulfate upon heating naphthionic acid, sulfanilic acid, and amino-Tobias-acid with α-naphthylamine.

If sodium naphthionate in neutral medium (naphthalene) rearranges to 1-naphthylamine-2-sulfonate without external exchange, but free naphthionic acid under these conditions as a result of hydrolytic decomposition forms only α-naphthylamine [1], then the conversion of the free naphthionic acid with α-naphthylamine (according to E.A. Shilov), which proceeds with an external exchange, has nothing in common with the rearrangements of the salts of the amino- and hydroxysulfonic acids. This was a process of reaction of radioactive sodium sulfate with α-naphthylamine ("baking" under ordinary conditions). Depending on the conditions, in this case of the reaction of naphthionic acid with α-naphthylamine it is possible to again form naphthionic acid or 1-naphthylamine-2-sulfonic acid.

From the data in the same Table 1 of E.A. Shilov's paper it follows that heating of α-naphthylsulfamate in naphthalene for 2 hours at 150° with α-naphthylamine and sulfuric acid led to the formation of 60% 1-naphthylamine-2-sulfonate and 7% of naphthionate with "considerable external exchange." Since it is known [1] that α-naphthylsulfamate in naphthalene at 150° is practically unchanged even after 2 or 3 hours, forming only 1% of 1-naphthylamine-2-sulfonate, the result of heating the above-mentioned mixture of α-naphthylsulfamate is not a consequence of rearrangement, but of "baking" of α-naphthylamine by polysulfates.

Summing up the above information, we consider that the conversion of the dry salts of amino- and hydroxyarylsulfonic acids on heating is a complex process, depending on the properties of the starting materials and their relationship to the external medium, and for naphthylamine- and naphtholsulfonic acids consists at least of two stages.

In the first stage, which appears to be strictly one of rearrangement, the sulfonates of naphthylamines or naphthols with sulfo groups in the α-position are converted to the corresponding naphthylsulfamates or salts of naphthol sulfates. The sulfonates of naphthylamines or naphthols with sulfo groups in the β-position are incapable of rearrangement.

α-Naphthylsulfamate or the salt of α-naphthol sulfate because of their lability can easily proceed farther to 1-naphthylamine-2-sulfonate, or 1-naphthol-2-sulfonate.

Similarly, reactions with added phenylamines or phenols proceed with the migration of sulfonate groups from one molecule to another. The nature of the sulfonates formed in this way depends on the properties and the proportions of the starting sulfonate and the additive.

In the second stage, which takes place under rather severe conditions of high temperature and acid medium, the naphthylamine- and naphtholsulfonates, and also the naphthylsulfamates and salts of naphthol sulfates (among them β-naphthylsulfamate and the salt of β-naphthol sulfate which are stable in the first stage) undergo partial breakdown and hydrolysis. The resulting naphthylamines or naphthols, and also the naphthylsulfamates or salts of naphthol sulfates themselves are sulfonated ("baked") to the corresponding salts of naphthylamine- or naphtholsulfonic acids with the sulfo group in the β-position, with the formation of compounds that are more stable under the conditions in question. "Baking" is especially favored by optimal concentration and composition of the polysulfates.

EXPERIMENTAL

(with the collaboration of V.D. Vitkina)

Starting materials. 1) Sodium salt of 2-naphthylamine-1-sulfonic acid, imported, 86.9% (water 6.2%, mineral salts 6.9%). Solubility of the salt determined at 20°, 14.33 g in 100 ml water. 2) Sodium salt of β-naphthylsulfamic acid obtained by the sulfonation of β-naphthylamine with chlorosulfonic acid in chloroform [8]. Salt content 95.8% (by diazotization of the β-naphthylamine derived from hydrolysis of a weighed portion of the salt in 10% HCl at 100° for 45 minutes). Solubility of the salt determined at 20° was 2.77 g in 100 ml water. 3) Naphthalene, technical grade 1 (solidification temperature 79.5°). 4) Sand, quartz, fine, dried and calcined, SiO_2 content 98%.

Identification of components of the reaction mass was carried out in the following manner: β-naphthylamine and naphthalene were determined by direct extraction of the reaction mass with dry benzene. After evaporation of the benzene, the dry residue was treated with dilute hydrochloric acid, filtered off from the naphthalene, and the quantity of β-naphthylamine determined by titration with a 0.1 N solution of nitrite. As a control in some experiments β-naphthylamine was isolated in the dry form (m.p. 104-108°) and weighed. The residue from the extraction of the reaction mass with benzene was dissolved in 100 ml of 10% hydrochloric acid, filtered off from the insoluble portion, and heated in a round-bottomed flask on a boiling waterbath for 45 minutes with a reflux condenser (to hydrolyze the naphthylsulfamic acid). The hydrolyzate obtained was neutralized with a concentrated solution of sodium hydroxide. The precipitate that had separated out was extracted with benzene. After evaporation of the solvent, the extract was treated with dilute hydrochloric acid and the β-naphthylamine in the solution was titrated with 0.1 N solution of nitrite, calculating the result in terms of the sodium salt of β-naphthylsulfamic acid.

The aqueous alkaline mother liquor was made acid to congo paper with hydrochloric acid and the amount of the salts of 2,1- and 2,6-naphthylaminesulfonic acids in the solution was determined by titration with 0.1 N nitrite solution. The residue from the first treatment of the reaction mass with benzene which did not dissolve in hydrochloric acid represented the unchanged starting salt of 2-naphthylamine-1-sulfonic acid, or the salt of 2-naphthylamine-6-sulfonic acid, or a mixture of both salts with carbon (also sand in experiments using the latter). The salts of the naphthylaminesulfonic acids were purified of carbon and sand by solution in boiling water. The carbon was separated from the sand by washing and decantation, dried, and weighed. In the solution the amount of naphthylaminesulfonic acids was determined by titration with 0.1 N nitrite solution. In parallel experiments cleavage of the naphthylaminesulfonic acids was carried out. Both the starting sodium salt of 2-naphthylamine-1-sulfonic acid and that isolated in the experiments easily formed 1-bromo-2-naphthylamine, m.p. 63° [9], upon treatment in aqueous solution with bromine water, and both were slowly hydrolyzed by heating in 30-50% sulfuric acid, and formed an insoluble crystalline diazo compound of a lemon-yellow color; on coupling with diazobenzene they yielded a dye (m.p. 103°) identical in its properties with phenylazo-β-naphthylamine [10].

The sodium salt of 2-naphthylamine-6-sulfonic acid isolated in a number of the experiments dissolved in water with a blue fluorescence, crystallized in needles, and yielded a diazo compound soluble in water. Upon treatment with bromine water in aqueous solution it formed a precipitate that dissolved on heating. In the mother liquor from the bromination, in contrast to the products of the analogous conversion of 2-naphthylamine-1-sulfonic acid, $SO_4^{=}$ ions were not detected. By diazotization of the sodium salt of the naphthylaminesulfonic acid and replacement of the diazo group with chlorine, the sodium salt of the chloronaphthylsulfonic acid was obtained which was converted by treatment with PCl_5 to 2,6-dichloronaphthalene (m.p. 136°), showing that the naphthylaminesulfonic acid obtained was the 2,6-isomer.

SUMMARY

1. The dry salt of 2-naphthylamine-1-sulfonic acid rearranges at comparatively low temperatures (100-170°) to the salt of β-naphthylsulfamic acid, which is stable in a soda medium.

2. At high temperatures the dry salt of 2-naphthylamine-1-sulfonic acid passes through a stage of rearrangement to the β-naphthylsulfamate, and the latter goes directly to the salt of 2-naphthyl-6-sulfonic acid. This promotes an increase in the concentration of polysulfates in the reaction mixture.

3. A general scheme has been proposed for the conversion of the dry salts of the amino- and hydroxyarylsulfonic acids by heating, which includes the rearrangement of the sulfonate group with the formation of naphthylsulfamates or salts of the naphthol sulfates and "baking" of them or of their hydrolysis products to new, more stable naphthylamine- or naphtholsulfonates.

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INVESTIGATIONS IN THE NAPHTHALENE SERIES

XVI. THE CONVERSION OF THE SALT OF 2-NAPHTHOL-6-SULFONIC ACID INTO THE SALT OF 2-NAPHTHOL-7-SULFONIC ACID

V.V. Kozlov and G.G. Yakobson

It has previously been stated [1] that dry salts of sulfonic acids of naphthylamines or naphthols which have a sulfo group in the β-position cannot undergo rearrangement.

At the same time, in an acid medium and at a high temperature, sulfonates of this type can undergo hydrolysis phenomena and fresh sulfonation "baking" with polysulfates which are more stable under these conditions. In order to check these suppositions, we investigated the behavior of a number of dry sulfonates of naphthylamines and naphthols whose conversion under heating was unknown.

In this article we give data on the behavior of the dry sodium salt of 2-naphthol-6-sulfonic acid during heating.

As we have shown [2], the salt of 2-naphthol-6-sulfonic acid was the final product of the conversion during heating in sand at 180-230° of the salt of 2-naphthol-1-sulfonic acid and also of the β-naphthol sulfate at 180-200°.

2 g of the sodium salt of 2-naphthol-6-sulfonic acid was heated in a medium of naphthalene or sand in a 100 cc round-bottomed flask with a reflux condenser, the flask being immersed in a metal bath and carbon dioxide passed through slowly [3].

In the initial heating stage drops of water, which rapidly evaporated, condensed on the walls of the flask and the condenser. Within 20-30 minutes from the commencement of heating, the reaction mass began to darken and traces of β-naphthol began volatilizing on the walls of the flask and the condenser. After the completion of heating, the reaction mass showed a slightly acid reaction to congo paper. There was an odor of sulfur dioxide.

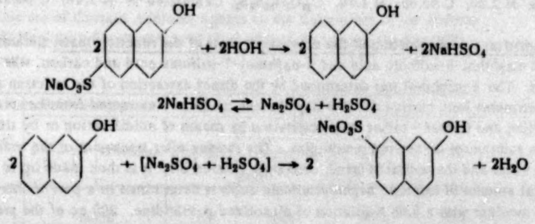
The separation of the salt of 2-naphthol-6-sulfonic acid from the 2-naphthol-7-sulfonic acid found in the reaction mass was based on the different solubilities of their disodium salts (the naphtholate-sulfonates) in 90% alcohol [4].

Heating the sodium salt of 2-naphthol-6-sulfonic acid in naphthalene up to 220° does not lead to a change in the latter and is accompanied only by a slight formation of β-naphthol. Even at 210°, however, the heating of this salt in sand does not lead to the appearance of traces of the salt of 2-naphthol-7-sulfonic acid detected by dark-blue coloration in a neutral solution of ferric chloride. Heating the sodium salt of 2-naphthol-6-sulfonic acid in sand at 280° for 4 hours leads to the appearance in the reaction medium of approximately equal amounts of the salt of 2-naphthol-6-sulfonic acid (48.4%) and the salt of 2-naphthol-7-sulfonic acid (41.3%). The increase of the heating time to 8 hours and the temperature to 330° results in a 10-15% increase in the amount of the salt of 2-naphthol-7-sulfonic acid with a corresponding reduction in the amount of the 2,6-isomer. With a further increase of the temperature to 350° the amount of both salts is reduced. Heating the pure salt of 2-naphthol-7-sulfonic acid under these conditions shows the considerable stability of this salt.

The fact that during heating in naphthalene the salt of 2-naphthol-6-sulfonic acid is not converted into the salt of 2-naphthol-7-sulfonic acid indicates that direct migration of the sulfonate group from one position of the ring to another does not take place here. In addition, no intermediate products of a possible rearrangement, e.g., β-naphthol sulfate, were found.

The formation of appreciable quantities of β-naphthol whenever the salt of 2-naphthol-6-sulfonic acid is heated and the presence of acidity in the reaction mass are, on the one hand, the result of the relative thermal instability of the salt of 2-naphthol-6-sulfonic acid, and on the other hand, a consequence of the hydrolytic action of water formed during the partial decomposition of the substance. The process of the conversion of the salt of 2-naphthol-6-sulfonic acid into the salt of 2-naphthol-7-sulfonic acid is very similar to the process of formation of the salt of 2-naphthol-6-sulfonic acid during heating of the dry salt of 2-naphthol-1-sulfonic acid [2] and is also analogous to the conversion of the salt of 2-naphthylamine-1-sulfonic acid into the salt of 2-naphthylamine-6-sulfonic acid [1].

Since it was established by our investigations [2, 5] that neither bisulfate nor pyrosulfate form sulfonic acids with α- or β-naphthols, the only possible way in which the new sulfonic acid is formed during heating of the salt of 2-naphthol-6-sulfonic acid must be the process of "baking" of β-naphthol with polysulfates according to the system



The formation of bisulfate and sulfuric acid, necessary for the formation of polysulfates, during similar processes of heating the dry salts of naphthylamine- and naphtholsulfonic acids has been confirmed by various investigators [3, 6].

Heating the salt of 2-naphthol-6-sulfonic acid in sand in the presence of alkali arrests the conversion and only β-naphthol is formed; the addition of bisulfate or drops of sulfuric acid, however, assists its conversion to the salt of 2-naphthol-7-sulfonic acid (Table 2). The action of these addition agents is evidently perfectly similar to the action of those employed in the conversion of the salts of 2-naphthol-1-sulfonic acid [2] and 2-naphthylamine-1-sulfonic acid [1], where the phenomenon of "baking" with polysulfates was found.

Heating free 2-naphthol-6-sulfonic acid in naphthalene and sand has not been found to result in the formation of a new substance. As a result of the alteration in the composition of acid agents during the hydrolysis and decomposition of the substance (sulfuric acid being obtained instead of polysulfate) the process of fresh sulfonation after hydrolysis leads to a different product than that obtained by "baking" i.e., the initial 2-naphthol-6-sulfonic acid.

The significance of the specific composition of the acid agents during "baking" is known from a number of processes, carried out in practice, including, for example, baking of naphthylamine with sulfuric acid to give naphthionic acid and with polysulfates to give 1-naphthylamine-2-sulfonic acid.

In conclusion it may be mentioned that the secondary process of sulfonation by polysulfates ("baking"), observed during heating of the dry salts of many naphthylamine- and naphtholsulfonic acids [1], usually give results different from those obtained with ordinary sulfonation by sulfuric acid because of the conditions of interaction of the reacting substances. The process may take place stepwise, passing through stages of hydrolysis and fresh "baking." The increase in the concentration and alteration of the composition of the polysulfates and also a high temperature assist the trend of the sulfonic group to occupy the nonquinoid positions of the naphthalene molecule (the 7-position for β-naphthol or β-naphthylamine and the 6-position for α-naphthol or α-naphthylamine).

EXPERIMENTAL

The sodium salt of 2-naphthol-6-sulfonic acid (Schäffer's salt) was prepared by repeated recrystallization of the commercial product from water, conversion to the barium salt and then to the free acid by the addition of the theoretical amount of sulfuric acid. After it had crystallized out from a concentrated solution the free acid was recrystallized from concentrated hydrochloric acid. It is in the form of platelets with a m.p. of 123° [7]. The salt formed with benzyl thiourea has a m.p. of 218° [9]. From a solution of 2-naphthol-6-sulfonic acid neutralized with caustic soda the sodium salt of this acid is precipitated on evaporation and the latter is again recrystallized from water and dried at 105°. The content of this acid is 92.5% and that of water 2.7% (by the carbide method).

The sodium salt of 2-naphthol-7-sulfonic acid was prepared by recrystallization of the commercial product. The content of the salt is 86% and that of water 2.5% (by the carbide method).

Free 2-naphthol-7-sulfonic acid [8] was obtained by a similar procedure to that for the above-mentioned isomer. The m.p. is 85°. The salt formed with benzyl thiourea has a m.p. of 185° (from 50% alcohol).

Found %: N 7.30; C 55.63; H 4.79. $C_{18}O_4H_{18}N_2S_2$. Calculated %: N 7.18; C 55.39; H 4.61.

The quantititave determination of the component parts of the reaction mass, including β-naphthol, the sodium salts of 2-naphthol-6-sulfonic acid and 2-naphthol-7-sulfonic acid and carbon, was carried out in the following manner. The β-naphthol was determined by the direct extraction of the reaction mass with benzene, and, where the experiments were carried out in a naphthalene medium – extracted from benzene again and 2N alkali hydroxide solution and further – either by precipitation by means of acidification or by titration in an alkaline medium with a solution of diazotized p-toluidine. The residue after treatment of the reaction mass with benzene is dissolved in water and the sediment (sand, carbon) is filtered off; it is then made up to 250 cc in a measuring flask. The total amount of isomeric naphthylsulfonic acids is determined in a part of this solution by coupling in an alkaline medium with a 0.05 N solution of diazotized p-toluidine. 200 cc of the prepared solution is treated with caustic soda solution until it gives a strongly-alkaline reaction with litmus and is then evaporated to a sirupy consistency. The mass is mixed with 100 cc of alcohol and the undissolved part is filtered off. The 2-naphthol-7-sulfonic acid salt content of the solution is determined by coupling in an alkaline medium with diazotized p-toluidine. From the solution containing the 2-naphthol-6-sulfonic acid salt it is easy to isolate the salt of benzyl thiourea which after crystallization has a m.p. of 218° and shows no depression of the melting point in a mixed melt with the pure benzyl thiourea salt of 2-naphthol-6-sulfonic acid.

TABLE 1

Results of the Analyses of Artificial Mixtures of the Sodium Salts of Naphtholsulfonic Acid

Grams of salt taken			Grams of salt obtained		
2,6-acid	2,7-acid	total	2,6-acid	2,7-acid	total
0.876	–	0.876	0.800	0.036	0.836
–	0.396	0.396	0.03	0.390	0.393
0.362	0.1596	0.5216	0.34	0.161	0.501

In a similar manner, from a solution containing the sodium salt of 2-naphthol-7-sulfonic acid the corresponding benzyl thiourea salt is isolated; after crystallization this has a m.p. of 185° and shows no depression of the melting point in a mixed melt with the pure compound.

Analysis of artificially composed mixtures of the salts of naphtholsulfonic acids by the method described gave satisfactory results (Table 1). Tables 2 and 3 give the results of experiments on the behavior of the salts with heating. The results of repeated experiments showed agreement.

TABLE 2

Influence of Temperature and Time on the Conversion of the Sodium Salt of 2-Naphthol-6-sulfonic Acid (2 g) with Heating with Sand (8 g)

Expt. No.	Temperature	Time heated (in hours)	Yield (in %)			
			β-naphthol	sodium salt		total
				2-naphthol-6-sulfonic acid	2-naphthol-8-sulfonic acid	
1	210°	4	4.0	94.9	Traces	98.9
2	220	8	4.1	94.9	Traces	99.0
3	280	4	6.8	48.4	41.3	94.5
4	280	8	8.0	37.5	43.7	89.2
5	330	4	5.1	37.5	44.9	87.5
6	330	8	1.5	32.7	38.8	73.0
7	350	4	0.5	30.3	42.4	73.2

TABLE 3

The Influence of Certain Addition Agents on the Conversion of the Sodium Salt of 2-Naphthol-6-sulfonic Acid (2 g) with Heating with Sand at 280° for 4 Hours

Expt. No.	Addition agents		Yield (in %)			
	amount (in g)	substance	β-naphthol	sodium salt		total
				2-naphthol-6-sulfonic acid	2-naphthol-7-sulfonic acid	
1	None		6.8	48.4	41.3	96.5
2	2	Na_2CO_3	10.5	85.5	Нет	96.0
3	2	$NaHSO_4$	3.2	37.8	52.0	93.0
4	0.06	H_2SO_4	5.3	43.6	44.3	93.2

SUMMARY

1. In an inert medium (sand) at high temperatures the dry salt of 2-naphthol-6-sulfonic acid is converted by hydrolysis and "baking" with polysulfates into the salt of 2-naphthol-7-sulfonic acid.

2. The process of hydrolysis and "baking" of naphthol- or naphthylamine-sulfonic acids can take place in stages. An increase in the concentration and the alteration of the composition of the polysulfates and, in addition, a high temperature assist the tendency of the sulfonate group to occupy the nonquinonoid positions of the naphthalene molecule.

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*Russian translation.

THE NITRATION OF EASILY-NITRATED AROMATIC COMPOUNDS

R.A. Slavinskaya

Many investigators [1-9] in studying the nitration of phenol and its derivatives with nitric acid in water, acetic acid, acetone, ethyl acetate and other solvents have found that this type of nitration possesses specific features in comparison with nitration by a mixture of sulfuric and nitric acids. The specific character is indicated primarily in the positive catalytic influence of the nitrous acid which is formed during the process of nitration as a result of the oxidation of the compound undergoing nitration by the nitric acid. In consequence, the nitration of aromatic compounds such as phenols and amines has an autocatalytic character. The authors referred to above found inhibition of the reaction and even its cessation as a result of the decomposition of the nitrous acid by urea, hydrazine sulfate and other reducing agents.

The kinetics of the nitration of phenols and amines have been investigated in detail in recent years by Ingold and his collaborators [10-14]. In studying the nitration of phenols and its derivatives in acetic acid by nitric acid of different concentrations, the authors found that two nitration mechanisms operate, the individual influence of these mechanisms depending on the concentration of the nitric acid. If the concentration of the nitric acid is high the nitrous acid and nitrates have an inhibiting effect on the rate of reaction; under these conditions the authors consider that the nitronium ion NO_2^+ is the nitrating agent. If the nitric acid concentration is low, nitrous acid acts as a positive catalyst and the reaction rate is directly proportional to the HNO_2 concentration. Although the latter remains constant prior to and after the reaction, the rate of nitration depends to a considerable extent on its initial value. Taking into account the rules of orientation, the authors consider that some type of positively charged ion, similar to the nitronium ion, must take part in the reaction; the nitrosonium ion NO^+, formed according to the system

$$HNO_2 + HNO_3 \rightleftarrows H_2NO_2^+ + NO_3^-$$

$$H_2NO_2^+ \rightleftarrows NO^+ + H_2O.$$

may be an example of these ions.

According to the representations of the authors the NO^+ interacts with the molecule of the aromatic compound according to the following system

$$ArH + NO^+ \xrightarrow[slow]{} ArHNO^+$$

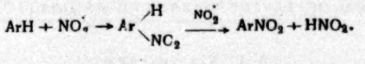
$$ArHNO^+ \xrightarrow[fast]{} ArNO + H^+$$

$$ArNO \xrightarrow[fast]{+NHO_3} ArNO_2 + HNO_2.$$

It was found that urea inhibits the reaction, whereas nitrates accelerate it.

In our opinion the conclusion made by British authors regarding a "special" mechanism of nitration of easily-nitrated aromatic compounds agrees with the view of A.I. Titov. A.I. Titov [15, 16] considers that, depending on the nitric acid concentration, it is necessary to distinguish "normal" nitration of aromatic compounds by nitronium ions and the "special" nitration mechanism by oxides of nitrogen.

On the basis of experiments on the nitration of various aromatic compounds (benzene, naphthalene, toluene, phenols, etc.) by nitric acid diluted with water, in the presence and absence of oxides of nitrogen, at room temperature and increased temperature in closed tubes and at normal pressure, the author found that the reaction does not take place in the absence of oxides of nitrogen. Nitration only occurs in the presence of oxides of nitrogen, the reaction rate being proportional to the concentration of the oxides of nitrogen in the reaction mixture. A.I. Titov, therefore, considers that the nitration of phenols by an aqueous solution of nitric acid takes place with the participation of oxides of nitrogen, the nitric acid molecules only acting as their supply source. The reaction proceeds according to the system



$$ArH + NO_2^{\cdot} \rightarrow Ar\begin{matrix} H \\ NO_2 \end{matrix} \xrightarrow{NO_2^{\cdot}} ArNO_2 + HNO_2.$$

In order to explain the nature of the nitrating agent in the nitration of easily-nitrated aromatic compounds we decided to study this type of nitration in an inert solvent, because the investigations of other authors were carried out in media which are bases with respect to nitric acid. As M.I. Usanovich and T. Sushkevich [17] showed, the yield of the nitration products, containing the nitro group either in the ring or the side chain (the authors nitrated toluene) decreases with the degree of dilution of the nitric acid by the inert solvent (ethyl nitrate, monochloracetic acid, etc.). On the basis of these data the authors drew the conclusion that the HNO_3 molecule itself does not nitrate. We considered it of interest to study the nitration of easily-nitrated aromatic compounds under the same conditions. We used ethyl nitrate as the inert solvent. We carried out the reaction with considerable dilutions of nitric acid, i.e., under conditions of minimum concentration of its ions or even when they were practically absent. Under these conditions we studied the nitration of phenol, nitrophenols, phenetole, naphthalene and, for purposes of comparison, acetanilide, which is usually nitrated by a mixture of nitric and sulfuric acids. To explain the influence of the oxides of nitrogen the nitration was carried out both in the absence and presence of urea nitrate, which, as is known, combines with oxides of nitrogen.

The solutions of nitric acid in ethyl nitrate were used at concentrations of 8 to 0.5% HNO_3, taking 1.5 moles of HNO_3 per mole of substance to be nitrated. The experiments were carried out at 18°.

As shown by the experimental data, the nitration of phenol by nitric acid in ethyl nitrate has an autocatalytic character, a fact which is clearly evident at a low concentration of the nitric acid. Rapid heating of the reaction mass, accompanied by the appearance of a red-brown color and the evolution of oxides of nitrogen, was observed shortly (10-30 sec) after the addition of the nitrating mixture to the phenol. The reaction takes place very rapidly. In the first 15 minutes up to 75-80% of the phenol is nitrated. During the course of the reaction o- and p-nitrophenols and 2,4-dinitrophenol are obtained. We studied the variation in the yield of the nitro derivatives as a function of the dilution of a constant amount of nitric acid with a varying amount of ethyl nitrate. As may be seen from Figure 1, the yield of o-nitrophenol remains almost constant with the decrease in the nitric acid concentration from 8 to 0.9%; the yield of p-nitrophenol increases initially, then falls, having a maximum value, corresponding to 0.9% HNO_3, while the yield of 2,4-dinitrophenol decreases slowly at first and then rapidly. This dependence of the yield of the reaction products on the concentration of the nitric acid is very similar to the kinetic relationship between the concentration of substances and time in the case of stepwise reactions. The data we obtained suggest that the dinitrophenol is obtained wholly by the nitration of the p-nitrophenol formed during the reaction whereas the o-nitrophenol does not undergo further nitration or is only nitrated extremely slowly. In order to confirm our supposition and define the kinetics of the nitration reaction of phenol with nitric acid in ethyl nitrate more accurately, we studied the relationship of the yield of the nitro derivatives with time at a constant HNO_3 concentration. We made a quantitative analysis of the reaction mixture at specific time intervals. Figure 2 gives the variation in the yield of the nitro deriva-

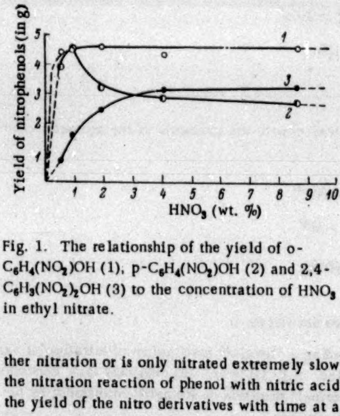


Fig. 1. The relationship of the yield of o-$C_6H_4(NO_2)OH$ (1), p-$C_6H_4(NO_2)OH$ (2) and 2,4-$C_6H_3(NO_2)_2OH$ (3) to the concentration of HNO_3 in ethyl nitrate.

tives with time during the nitration of 7.5 g of phenol by 8.2% HNO_3 (5.6 cc HNO_3 to 85 cc $C_2H_5ONO_2$) at 18°. From Figure 2 it is seen that the yield of o-nitrophenol increases rapidly in the first 15 minutes, then slowly, and after 60 minutes hardly varies. The yield of p-nitrophenol increases rapidly in the first 10 minutes and then begins to fall; after 120 minutes the fall in the yield of the nitro derivatives is insignificant. The yield of the dinitrophenol increases fairly rapidly for 120 minutes, then only slightly. This relationship of the yield of the reaction products with time indicates that under these conditions the dinitrophenol is formed by nitration of the p-nitrophenol while the o-nitrophenol evidently does not take part in the reaction.

The nitration of p- and o-nitrophenols separately under conditions similar to the nitration of phenol indicated that in actual fact the rate of nitration of p-nitrophenol is considerably higher than that for the o-isomer if the reaction rate is judged, with some approximation, from the yield of dinitrophenol in a specific time interval. For example, o-nitrophenol is only 6.5% nitrated by 8.6% HNO_3 for 2 hours at 18° whereas p-nitrophenol is 100% nitrated. The results of the nitration of o-nitrophenol are given in Figure 3, and those for p-nitrophenol in Table 1.

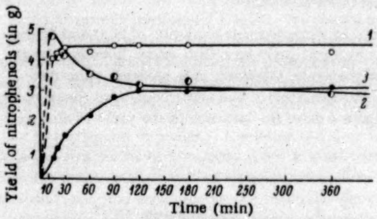


Fig. 2. The relationship of the yield of o-$C_6H_4(NO_2)OH$ (1), p-$C_6H_4(NO_2)OH$ (2) and 2,4-$C_6H_3(NO_2)_2OH$ (3) to time during nitration with 8.2% HNO_3 in ethyl nitrate.

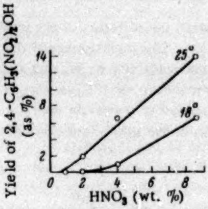


Fig. 3. The nitration of o-nitrophenol by solutions of HNO_3 in ethyl nitrate.

The experimental data show that in both instances the yield of dinitrophenol (and, therefore, also the mean reaction rate) is proportional to the HNO_3 concentration. From comparison of the yield of 2,4-dinitrophenol during the nitration of phenol and nitrophenols under identical conditions it is evident that more dinitrophenol is obtained in the nitration of phenol (Figure 1) than in the nitration of nitrophenols (Figure 3, Table 1), although the reverse result would be expected. We explain this result by the fact that evolution of heat takes place rapidly during the nitration of phenol and it is, therefore, difficult to maintain the temperature within the reaction mixture at 18°. A slight rise in temperature must, naturally, influence the yield of the reaction products. Evolution of heat was not observed during the nitration of nitrophenols. If, however, the temperature of the experiment is increased to 25° the yield of dinitrophenol in the nitration of o-nitrophenol (Figure 3) increases 2-2.5 times, and in the nitration of p-nitrophenol,3 times (Experiments Nos. 2 and 4, Table 1).

TABLE 1

The Nitration of p-Nitrophenol at 18° and 25°

Expt. No.	Concentration of HNO_3 (%)	Temperature	Yield of 2,4-dinitrophenol (as %)
1	8.6	1	100.0
2	1.0	1	32.2
3	1.9	1	1.6
4	4.0	2	90.0

Taking the nitration of p-nitrophenol as an example we investigated the influence of urea on the dinitrophenol yield. If the solution of nitric acid in ethyl nitrate is first boiled to remove oxides of nitrogen and added, after cooling, to the p-nitrophenol the dinitrophenol yield is considerably reduced. For example, 8.6% HNO_3, in the absence of urea nitrates p-nitrophenol 100% in 2 hours at 18°, but only 37% if urea is present. As far back as 1925, B.V. Tronov [19, 20] established that ethyl nitrate, by itself, does not nitrate even easily-nitrated compounds like anisole. We investigated the direct action of ethyl nitrate on phenol and obtained a negative result. Nitration of phenol with varying amounts of nitric acid but with the same volume of ethyl nitrate showed that the yield of the nitro derivatives is directly proportional to the amount of HNO_3 (Table 2).

TABLE 2

Nitration of Phenol by Nitric Acid Solutions in 81 cc of Ethyl Nitrate for 2 Hours

Expt. No.	Amount of HNO_3 (cc)	Yield (in g)		
		o-nitrophenol	p-nitrophenol	dinitrophenol
1	5.6	4.60	2.80	3.36
2	2.8	2.60	4.15	0
3	1.4	3.64	2.12	–
4	0	0	0	0

This again shows that the ethyl nitrate does not take part in the reaction.

As with phenol, the nitration of phenetole is accompanied by a considerable evolution of heat and tarring of the reaction mass. The replacement of the hydrogen of the hydroxyl group by a C_2H_5 group, however, leads to a reduction in the reactivity of the ring and the nitration of phenetole, therefore, only proceeds up to the formation of the mononitro-derivatives (we isolated p- and o-nitrophenetoles), and under conditions where phenol is 70% nitrated nitration of phenetole does not take place. Figure 4 shows the variation in the yield of nitrophenetoles as a function of the nitric acid concentration at 18°.

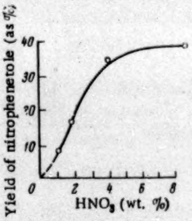


Fig. 4. Relationship of the yield of nitrophenetoles to the HNO_3 concentration in ethyl nitrate.

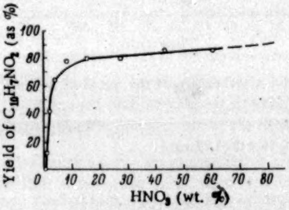


Fig. 5. Relationship to the yield of α-nitronaphthalene to the concentration of HNO_3.

From Figure 4 it is evident that with increasing concentration of nitric acid the yield of nitrophenetoles shows an initial rapid increase, but, beginning with a 4% concentration of the HNO_3 it is retarded.

Naphthalene is nitrated to α-nitronaphthalene. Even a 1.9% solution of nitric acid nitrates naphthalene 42% over a period of 2 hours. The relationship of the yield of nitronaphthalene to the nitric acid concentration is the same as for nitrophenols and nitrophenetoles: with decreasing nitric acid concentration the α-nitronaphthalene yield shows only a slight initial alteration, but commencing with 1.9% HNO_3 proceeds rapidly (Figure 5). The yield of α-nitronaphthalene is considerably reduced in the presence of urea. For example, whereas 40% HNO_3 nitrates naphthalene 80% over a period of 2 hours at 18° without urea, it is only nitrated 27% in the presence of urea.

Acetanilide is not nitrated under our conditions. Since the nitration of phenol, nitrophenols, phenetole, naphthalene and acetanilide was carried out in a solvent inert with respect to HNO_3 and at considerable dilutions, i.e., under conditions where nitric-acid ions (or nitronium ions) were practically absent, participation of these ions in the reaction was excluded. From the work of M.I. Usanovich and A.I. Titov it is known that molecular nitric acid by itself does not nitrate. Under our conditions oxides of nitrogen (NO_2) can be the only nitration agent. This is confirmed by the inhibitory action of urea, which decomposes oxides of nitrogen and nitrous acid, on the reaction rate. The reason why urea does not cause complete cessation of the reaction is evidently because it is not very soluble in ethyl nitrate and, therefore, does not completely decompose the oxides of nitrogen. Easily-nitrated aromatic compounds (phenol, naphthalene) are nitrated in ethyl nitrate but those substances (acetanilide) for which a mixture of nitric and sulfuric acid is used for nitration are not nitrated under these conditions.

In our opinion, therefore, the data on the nitration of phenol, nitrophenols, naphthalene, phenetole and acetanilide confirm the conclusion of A.I. Titov to the effect that in the nitration of easily-nitrated aromatic compounds by nitric acid, diluted with water (and, in our opinion, with other bases and inert solvents), oxides of nitrogen are the nitration agent.

EXPERIMENTAL

PREPARATION AND PURIFICATION OF REAGENTS

Anhydrous nitric acid was prepared by distilling HNO_3 (d 1.39) twice with an equal volume of H_2SO_4 (d 1.84), and then blowing dry air through in order to remove oxides of nitrogen [18]. The nitric acid obtained had a density of 1.517-1.520. The ethyl nitrate was made from nitric acid (d 1.39) and 96% ethyl alcohol; it had a b.p. of 84-84.5° (at 695 mm) and d 1.1102. The phenol used had a b.p. of 176-176.3° (at 697.4mm) and a m.p. of 45°. After recrystallizing twice from alcohol the o-nitrophenol had a m.p. of 45°. After recrystallizing from water acidified with hydrochloric acid, the p-nitrophenol had a m.p. of 112°. The phenetole was purified by distillation; b.p. 169-169.5° (700 mm). The "sublimed" grade of naphthalene was used; b.p. 80°. The acetanilide was purified by recrystallizing twice from water and had a m.p. of 112-113°.

The nitration of phenol. A solution of 5.6 cc HNO_3 (0.13 mole) in 75 cc of ethyl nitrate was added with stirring over a period of 7 minutes at 16° to a mixture of 7.5 g (0.078 mole) of phenol and 10 cc of ethyl nitrate. Since the reaction was vigorous and accompanied by evolution of heat, the temperature of the thermostat was somewhat modified and subsequently maintained constant at 18°. Evolution of oxides of nitrogen was observed simultaneously with the evolution of heat and turbulence of the mixture. After the reaction mixture had stood for 2 hours at 18° it was poured into water and repeatedly washed with a solution of alkali and water to remove excess nitric acid, after which it was dried over $CaCl_2$. The ethyl nitrate was evaporated off on a water bath and the residue steam-distilled to separate the o-nitrophenol. The p-nitrophenol and 2,4-dinitrophenol were separated by fractional crystallization from water. Since the solubility of 2,4-dinitrophenol in water is 3 times less than that of p-nitrophenol, the dinitrophenol crystallized first while the p-nitrophenol remained in solution. 4.60 g of o-nitrophenol, 2.80 g of p-nitrophenol and 3.36 g of 2,4-dinitrophenol were obtained.

Changes in the yield of nitroproducts in relation to the quantity of nitric acid, its concentration and time during nitration were studied. The results are shown in Figures 1 and 2, and Table 2.

The nitration of o-nitrophenol. A solution of 2.8 cc of HNO_3 in 41 cc of ethyl nitrate was added to 5.54 g of o-nitrophenol at 18°. We kept the reaction mass at 18° for 2 hours, after which it was poured into water, washed free of excess nitric acid and dried over $CaCl_2$. The ethyl nitrate was evaporated off on a water bath and the residue steam-distilled. The unreacted o-nitrophenol distilled over with the steam and the 2,4-dinitrophenol remained in the residue. 0.85 g of 2,4-dinitrophenol was obtained.

The variation in the yield of 2,4-dinitrophenol with the concentration of HNO_3 and temperature was studied. The results are given in Figure 3.

The nitration of p-nitrophenol was carried out under conditions similar to the nitration of o-nitrophenol. The 2,4-dinitrophenol was separated from the unreacted p-nitrophenol by fractional crystallization from water.

The variation in the yield of 2,4-dinitrophenol with the concentration of HNO_3, temperature and presence of urea was studied. The results are given in Table 1.

The nitration of phenetole. A solution of 5.6 cc of nitric acid in 73 cc of ethyl nitrate was added over a period of 7 minutes at 17° to a mixture of 10 cc of phenetole and 8 cc of ethyl nitrate, after which the temperature of the thermostat was increased to 18° and maintained constant for 2 hours. When the nitric acid was poured into the phenetole slight evolution of heat and darkening of the phenetole were observed. After standing for 2 hours the mass was washed with alkali solution and water to remove the excess nitric acid and dried over calcium chloride. The ethyl nitrate was evaporated off on the water bath and the residue fractionally distilled with steam to remove the tarry products and separate the nitro derivatives. p- and o-nitrophenetoles were isolated from the reaction products; the total yield was 4.47 g.

The variation in the yield of the nitro derivatives with the concentration of HNO_3 is given in Figure 4.

The nitration of naphthalene. A solution of 5.6 cc of nitric acid in 73 cc of ethyl nitrate was added at 18° to a mixture of 10.21 g of naphthalene and 8 cc of ethyl nitrate. The reaction mass was maintained at 18° for 2 hours after which it was washed with alkali solution and water and dried over $CaCl_2$. The ethyl nitrate was evaporated off on the water bath and the residue boiled with water to remove naphthalene. The α-nitronaphthalene, which was recrystallized from alcohol, remained in the residue. The nitration results are given in Figure 5.

The nitration of acetanilide was carried out in a similar manner to the nitration of naphthalene. In order to separate the o-nitroacetanilide the mixture of the reaction products was steam distilled and fractionally crystallized to isolate the p-nitro derivative. No nitro derivatives were obtained and acetanilide is, therefore, not nitrated in ethyl nitrate.

SUMMARY

1. The nitration of phenol, o-nitrophenol, p-nitrophenol, phenetole, naphthalene and acetanilide by nitric acid in ethyl nitrate (inert solvent) at 18° was studied.

2. The nitration of phenol under the conditions indicated takes place with formation of o- and p-nitrophenols and 2,4-dinitrophenol. The form of the curves of the relationship of the yield of the reaction products with time indicates that of the mononitrophenols formed during the nitration of phenol only p-nitrophenol is nitrated further to dinitrophenol while the o-isomer evidently does not take part in the reaction.

3. p-Nitrophenol is nitrated in ethyl nitrate to dinitrophenol with considerably more rapidity than o-nitrophenol. Phenetole and naphthalene are nitrated with formation of mononitro derivatives. Under similar conditions acetanilide does not take part in the nitration reaction.

4. Under these conditions oxides of nitrogen are the nitration agent for easily-nitrated aromatic compounds.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

LXXIV. THE INFRARED SPECTRA AND REACTIVITY OF VINYLACETYLENE HYDROCARBONS

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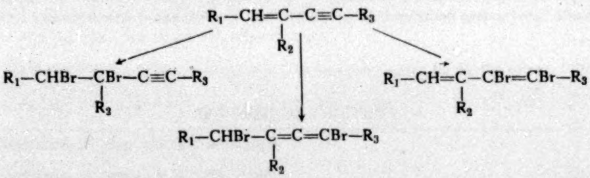
In preceding communications of our laboratory it was shown that vinylacetylene hydrocarbons behave differently with respect to bromine according to their structure.

Vinylacetylene (R_1, R_2, R_3 = H) forms all three possible dibromides with a predominance of the isomers with allene and 1,3-diene structures [1].



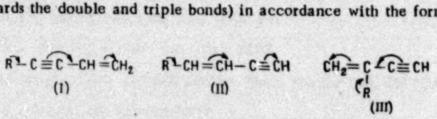
$R_1-CH=C(R_2)-C\equiv C-R_3$
$R_1-CHBr-CBr(R_2)-C\equiv C-R_3$
$R_1-CH=C(R_2)-CBr=CBr-R_3$
$R_1-CHBr-C(R_2)=C=CBr-R_3$

Homologs of vinylacetylene with radicals at the triple bond (R_1 and R_2 = H, R_3 = alkyl, type I) give principally acetylene dibromides with a slight admixture of dienes. Allene dibromides were not found [2]. Homologs with a radical at the terminal atom of a double bond (R_1 = alkyl, R_2 and R_3 = H, type II) give allene dibromides with an admixture of dienes. Acetylene dibromides were not found [3]. Finally, hydrocarbons with a radical at the central atom of an enoid group (R_2 = alkyl, R_1 and R_3 = H, type III) form principally acetylene dibromides with an admixture of diene and allene dibromides [4].

Vinylacetylene hydrocarbons with isolated multiple bonds ($CH_2 = CH - CH_2 - C \equiv CH$ [5] and $CH_2 = CH - CH_2 - C \equiv C - CH_3$ [6]) add bromine at the double bond.

At the same time all the acetylene hydrocarbons listed add hydrogen and hydrogen halides at the acetylene bond [6-9].

The particular features in the behavior of vinylacetylene homologs of different structure were explained by the possibility of migrations of electrons in the molecules of these compounds under the influence of radicals in two opposed directions (towards the double and triple bonds) in accordance with the formulas:



Migrations of this type of the electron cloud must have found their counterpart in the physical properties of these substances: dipole moments, interatomic distances, vibration spectra.

There are no data in the literature on the dipole moments of vinylacetylene hydrocarbons.

Expt. No.	Substance	$^{\nu}$CH			$^{\nu}$C=C	$^{\nu}$C≡C	$^{\delta}$CH			$^{\delta}$CH		2 × $^{\delta}$CH
		≡CH	=CH$_2$	=CH—			—CH$_2$—	—CH$_3$	=CH$_2$	=CH—	=CH$_2$	
1	$CH_2{=}CH{-}C{\equiv}CH$	3300	3105	3030	1610	2114	—	—	1412	971	928	1859
2	$CH_3{-}CH{=}CH{-}C{\equiv}CH$ . .	3300	—	3040	1623	2114	—	1445	—	955	—	—
3	$C_2H_5{-}CH{=}CH{-}C{\equiv}CH$ . .	3300	—	3040	1623	2114	1468	1445	—	955	—	—
4	$CH_2{=}C(CH_3){-}C{\equiv}CH$ . .	3300	3105	—	1621	2114	—	1451	1412	—	903	11818
5	$CH_2{=}C[C(CH_3)_3]{-}C{\equiv}CH$	3300	3105	—	1621	2123	—	(1484)	(1471)	—	908	1825
6	$CH_3{-}CH{=}C(CH_3){-}C{\equiv}CH$	3300	3115	3040	1616	2114	—	1456	1414	—	911	1815
7	$CH_2{=}CH{-}C{\equiv}C{-}CH_3$ . . .	—	3115	3030	1608	2257	—	1445	1418	976	920	1852
8	$CH_2{=}CH{-}C{\equiv}C{-}C_2H_5$ . .	—	3115	3040	1608	2257	1468	1445	1422	980	919	1852
9	$CH_2{=}CH{-}C{\equiv}C{-}C_3H_7$ . .	—	3115	3021	1608	2252	1460	1441	1422	979	919	1825
10	$CH_2{=}CH{-}C{\equiv}C{-}C_4H_9$ . .	—	3105	3021	1608	2252	1460	1441	1422	974	917	1832
11	$CH_2{=}CH{-}CH_2{-}C{\equiv}C{-}CH_3$	—	3096	3021	1645	2268	—	—	1429	994	917	1852

The interatomic distances were measured for two hydrocarbons of this type – vinylacetylene [10, 11] and vinylmethylacetylene [12]. The contraction in the = C – C ≡ distance, found in both instances, can serve as a proof of the presumed migration of the electron cloud but it gives no indication of the direction of this migration. In addition, in the vinylmethylacetylene molecule the C – C ≡ link shows a marked contraction which may be considered as direct proof in favor of the existence of the effect in question. In the opinion of certain authors, however, the contraction of the distances is not necessarily a result of the migrations of the electrons and may be caused by differences in the state of the carbon atoms, forming these bonds [13].

To find further physical confirmations of the presence of electron migrations in the molecules of vinylacetylene hydrocarbons of various structure in the sense of the above-mentioned formulas (I-III) we investigated the infrared spectra of 11 substances in the 3-15μ region. The literature gave data only for vinylacetylene [14]. The curves of the transmission spectra which we obtained are given in Figure 1. The principal absorption bands are given in Table 1. The data available in literature for vinylacetylene, divinyl, and also for saturated, ethylene- and acetylene hydrocarbons [15-18] were taken as the basis for the allocation of the frequencies.

The general structural laws established in the last 10 years for the infrared spectra of hydrocarbons of the aliphatic series were also observed in a number of vinylacetylene hydrocarbons.

Vibrational frequencies of the CH group. The same frequency – 3300 cm^{-1} – corresponds to the CH-vibrations of the terminal acetylene group in all vinylacetylene hydrocarbons which are monosubstituted acetylenes. The intensity of this frequency is higher in the spectra of type (II) hydrocarbons than for type (III). Hydrocarbons of different structure do not show absorption in this region.

Two frequencies are found for all compounds having a vinyl group: 3110 ± 5 and the more intense 3030 ± 10 cm^{-1}. The first of these corresponds to the CH = vibrational frequency of the $CH_2{=}$ group, the second to the CH= group. Hydrocarbons with the $CH{=}CH{-}$ group do not show absorption in the 3110 cm^{-1} region, while on the contrary, hydrocarbons with the $CH_2{=}CR{-}$ group do not show absorption in the 3030 cm^{-1} region. Conjugation with an acetylene bond leads to the displacement of these frequencies in comparison with olefines in the short-wave region, by approximately 20 cm^{-1}. The same phenomenon occurs in a number of 1,3-dienes [18].

Apart from the frequencies noted in the spectra of vinylacetylenes there are from one to five frequencies which also correspond to vibrational frequencies of the CH group.

Vibrational frequencies of the C=C– group. The frequency of the double bond (1608 cm^{-1}) remains constant for vinylacetylene and all the vinylacetylenes. For the alkenylacetylenes (types II and III) this frequency is 12-15 cm^{-1} higher. The tertiarybutyl radical reduces the frequency of the double bond in comparison with the methyl radical. As a result of conjugation with a triple bond the frequency is always 30-40 cm^{-1} lower than with olefines and unconjugated vinylacetylenes.

The intensity of the bands, corresponding to a double bond, are very different, according to the particular structure of the hydrocarbon. Alkenylacetylenes of the straight chain type (type II) show comparatively weak absorption in this region. On the contrary, this band is sharply defined in the spectra of vinylacetylenes (type I) and isoalkenylacetylenes (type III), i.e., in the very substances which add bromine at the double bond.

Vibrational frequencies of the C≡C− group. All vinylacetylene hydrocarbons with a terminal acetylene group show absorption in the 2115 cm^{-1} region. This frequency is 10-15 cm^{-1} lower than with acetylenes. Conjugation, therefore, leads to a considerable reduction in the frequency of the triple bond compared to the double.

Conjugation with a double bond causes a marked increase in the intensity of the band corresponding to a triple bond. A still greater increase in the intensity is found as a result of the introduction of radicals into the molecule. In alkylacetylenes (type II) which add bromine at the triple bond, the intensity of the frequency of the acetylene bond is higher than for type (III) hydrocarbons, which add bromine at the double bond.

Displacement of the triple bond towards the middle of the molecule generally leads to a sharp decrease in the intensity of its corresponding band in the infrared spectra. This rule is not observed in the vinylacetylene hydrocarbons which we investigated: the intensity of the band, corresponding to a triple bond, remains high.

Isomeric vinylacetylene hydrocarbons which are doubly-substituted acetylenes with conjugated and unconjugated systems of multiple bonds, have absorptions showing a variation of only 10-15 cm^{-1} in this region. Vinylalkylacetylenes absorb at 2255 ± 3 cm^{-1}, allylmethylacetylene at 2268 cm^{-1}. Doubly-substituted acetylenes are characterized by frequencies in the region of 2230-2260 cm^{-1}. In consequence, here also, if the reduction in the frequency of the triple bond is observed at all it is very slight.

It must be pointed out, however, that the problem of the origin of the frequencies characterizing a doubly-substituted acetylene group is not fully resolved. In the 2100-2300 cm^{-1} region several frequencies whose origin is not completely established are generally found for these compounds [16, 17]. In the case of vinylacetylenes there are also several frequencies in this range. The maximum frequencies (after those noted above) are at about 2212 cm^{-1}.

Planar deformation vibrations of the CH group. In all the vinylacetylene hydrocarbons the deformation vibrations of the CH_2= group are characterized by frequencies at 1410-1430 cm^{-1}. Introduction of a methyl group in the molecule is accompanied by the appearance of frequencies of 1440-1455 cm^{-1} in the spectrum. An increase of alkyl by one or more $-CH_2-$ groups leads to the appearance of a higher frequency of about 1465 cm^{-1}.* Similar phenomena are also found in the spectra of other hydrocarbons.

All the investigated hydrocarbons show absorption at 1284 ± 12 cm^{-1}, and also have individual, not always well-differentiated frequencies of about 1380, 1368 and 1330 cm^{-1}.

The intensity of the highest frequencies of deformation CH-vibrations generally exceeds the intensity of the other frequencies which, particularly in the case of the vinylalkylacetylenes, are found as peaks on this main absorption band. The frequency of 1284 cm^{-1} is better than the others.

Nonplanar deformations of the CH group. Of this frequency group, two bands which help to resolve the problem of olefine group structure, are of the greatest interest [17-19].

Vinylacetylene hydrocarbons which possess a vinyl group always have two very intensive absorption bands of 976 ± 5 and 922 ± 6 cm^{-1} in the infrared spectra. Hydrocarbons with a CH_2=C group also show absorption in the 905 ± 3 cm^{-1} region but hydrocarbons with a −CH=CH− group only in the 955 ± cm^{-1} region.** In comparison with ethylene hydrocarbons the value of the higher frequency of the CH=C− group is reduced by approximately 20 cm^{-1}, that of the lower frequency of the CH_2 group is increased by 10-20 cm^{-1}. Conjugation with a triple bond, therefore, leads to a levelling out of the frequencies of the nonplanar deformation vibrations of these two groups. The intensity of these vibrations is higher for compounds of the (II) and (III) type than for the (I) type.

The absorption bands of about 1030 cm^{-1} and in the region of 660-740 cm^{-1} may evidently be included in this group. Since frequencies corresponding to vibrations of the carbon chain can be found in this region, the attribution of the frequencies is of considerable difficulty.

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*The introduction of a CH_2 group between multiple bonds is not accompanied by the appearance of this frequency.

**The appearance of an intensity with a frequency of 955 cm^{-1} in the spectra indicates a transconfiguration, in the main part, at least, of the investigated hydrocarbons.

Composite frequencies. Ethylene hydrocarbons are characterized by the presence of a fairly intensive frequency in the 1800-1850 cm^{-1} region, which is generally considered as an overtone in the nonplanar deformation frequency of the CH_2 group [16]. Vinylacethylene hydrocarbons, containing a $CH_2=$ group, and, therefore, showing absorption in the 900-930 cm^{-1} region, also show intense absorption in the 1818-1852 cm^{-1} region.

Acetylene compounds are characterized by fairly intense absorption at 1650-1700 cm^{-1}, whose origin has not been explained [20]. Vinylacetylene hydrocarbons with a terminal acetylene group, in the majority of instances have two bands in this region – at about 1650 and 1720 cm^{-1}. Only one frequency (about 1660 cm^{-1}), which usually occurs as a peak on the absorption band, caused by the presence of the double bond, is found in the case of vinylalkylacetylenes. These are evidently composite frequencies caused by the superposition of the deformation frequencies of the acetylene group on some other frequencies.

Composite frequencies are also found in other regions of the spectra of vinylacetylene hydrocarbons. They are particularly frequent in the 1900-2800 cm^{-1} range. These frequencies are generally weak or very weak.

The data provided on the infrared spectra of vinylacetylene hydrocarbons lead to the conclusion that the position of the absorption bands, corresponding to the multiple bonds, has no connection at all with the rules which we found to govern the reaction capacity of these substances. The intensity of the absorption bands of multiple bonds, however, is evidently associated with the reactivity. In actual fact, an increase in the frequency intensity of the double bond and a decrease in that of the triple bond is found as a result of the conversion of type (II) hydrocarbons, which add bromine at the triple bond, to type (III) hydrocarbons, which add bromine at the double bond (with identical character of substitution for the acetylene group). Since the intensity of the absorption vibration bands in infrared spectra is determined by the variations in polarity along the coordinate it is possible to draw the conclusion that the order in which bromine is added (point of initial attack) depends on the polarity of the bonds.

Migration of the electron cloud towards an acetylene group or away from it also influences the intensity of bands of vibrations with respect to the $\equiv C-H$ bond. It is considerably more in the case of hydrocarbons of type (II). As a result of migration of the electron cloud to the end of the acetylene group the alteration in the polarity with extensions of the $\equiv C-H$ bond will, naturally be greater, which in turn leads to an increase in the absorption intensity in this region.

The measurements of interatomic distances and infrared spectra are, therefore, in agreement with the suggestion of the migrations of electrons in molecules of vinylacetylene hydrocarbons under the influence of radicals in conformity with formulas (I, II and III).

EXPERIMENTAL

The infrared spectra were obtained by an IKS-2 biradiant spectrograph with a wavelength scanner, employing a lithium fluoride prism for the 3-5μ range, and a sodium chloride prism for the 5-15μ range, with a layer thickness of 0.102 mm and, in addition, with layer thicknesses of 0.03 and 0.25 mm for individual sections.* The vinylacetylene was photographed in solution (in CCl_4).

The alkenylacetylenes (3-penten-1-yne and 3-hexen-1-yne) were obtained by distillation of the p-toluenesulfonates of the corresponding alkylpropargyl alcohols with alkali [21]. These alcohols were prepared from propargyl bromide and the corresponding aldehydes by the action of zinc (under the conditions of the Reformatsky reaction) [22].

The isoalkenylacetylenes were obtained by catalytic dehydration of the corresponding tertiary alcohols over aluminum phosphate at 300° (3-3-methylbuten-1-yne [23] and 3-3-methylpenten-1-yne [24]) or over anhydrous magnesium sulfate at 300° (3'3'-dimetho-3-3-ethylbuten-1'-yne)[25]. The initial alcohols were prepared by condensation of the corresponding ketones (acetone, methylethylketone and pinacoline) with sodium acetylide in liquid ammonia.

Vinylalkylacetylenes (1-penten-3-yne, 1-hexen-3-yne, 1-hepten-3-yne, 1-octen-3-yne) were obtained by the action of the corresponding alkyl bromides on sodium vinylacetylide in liquid ammonia [26].

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* The authors wish to express their thanks to M.S. Barvinok for permission to use the spectrograph.

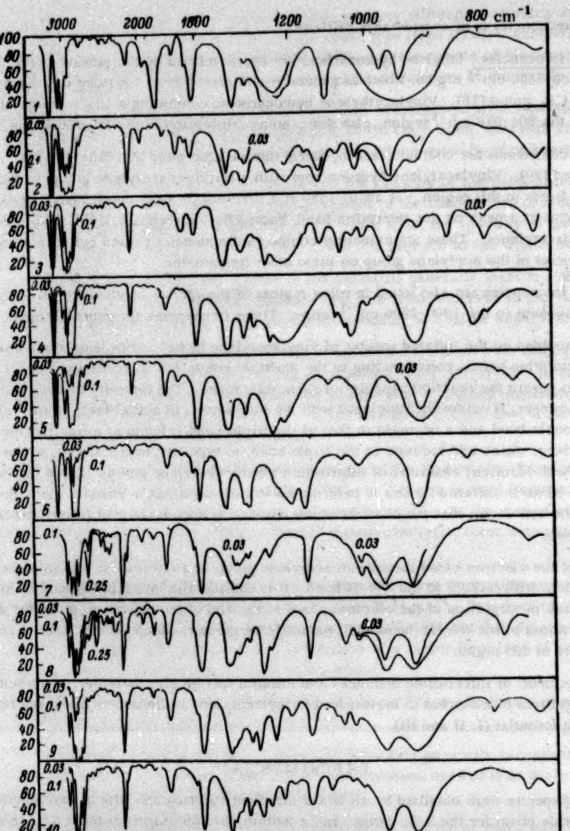

Fig. 1. Transmission spectra: 1) vinylacetylene (10% solution in CCl_4, thickness of layer, 1 and 0.5 mm); 2) 3-penten-1-yne (in this and subsequent compounds the thickness of the layer was 0.1 and 0.03 mm); 3) 3-hexen-1-yne; 4) 3-3-methylbuten-1-yne; 5) 3-3-methylpenten-1-yne; 6) 3-3-metho-3-3-ethylbuten-1-yne; 7) 1-penten-3-yne; 8) 1-hexen-3-yne; 9) 1-hepten-3-yne; 10) 1-octen-3-yne; 11) 1-hexen-4-yne.

Allylmethylacetylene was prepared by the action of allyl bromide on methylacetylene magnesium bromide in ether in the presence of cuprous bromide [6].

Before the experiments were commenced the hydrocarbons were distilled in a Widmer column (25 cc). The vinylacetylene used was also freshly distilled.

The constants of all the hydrocarbons used for this investigation did not differ in practice from those previously given in the literature. A composite table of the constants of these hydrocarbons will be given in the next communication.

Vinylacetylene.* 3.03 (v.s.), 3,22 (s), 3.26• (s), 3.30 (s), 3.44• (av), 3.49 (w), 3.74(w) , 3.79• (v.w.), 4.01 (v.w.), 4.18 (v.w.), 4.34 (v.w.), 4.73 (av), 5.20 (av), 5.38 (s), 5.77 (w), 6.03• (av), 6.21 (s), 7.09 (s), 7.37 (av), 8.06 (s), 9.12 (s), 10.30 (v.s.), 10.77 (v.s), 11.38 (av), 14.80 (av) μ.

3-Penten-1-yne. 3.03 (v.s), 3.29 (s), 3.35 (s), 3.40• (s), 3.43 (s), 3.50 (s), .65 (av), 3.84 (v.w.), 3.91 (v.w.), 4.05 (v.w.), 4.16 (v.w.), 4.73 (s), 5.02 (w), 5.52 (w), .82 (av), 6.02• (av), 6.16 (av), 6.92 (s), 7.23• (s), 7.33 (s), 7.81• (s), 8.19 (s), 8.61• (s), .94 (s), 9.31 (av), 9.73 (s), 10.47 (v.s.), 11.10 (av), 11.86 (av), 13.72 (s) μ.

3-Hexen-1-yne. 3.03 (v.s), 3.29 (s), 3.36 (s), 3.40 (s), 3.48 (s), 3.67 (av), 3.86 (v.w.), 3.93 (v.w.), 4.06 (v.w.), 4.18 (v.w.), 4.39 (v.w.), 4.73 (s), 5.02 (w), 5.32 (w), 5.63• (w), 5.88 (av), 6.02 (w), 6.16 (av), 6.81 (s), 6.92• (s), 7.18 (s), 7.70 (s), 8.10 (s), 8.61 (av?), 8.94 (s), 9.35 (s), 9.60 (av), 9.82 (av), 10.47 (v.s), 11.05 (w), 11.72 (av), 12.50 (av), 13.59 (s) μ.

3-3-Methylbuten-1-yne. 3.03 (s), 3.22 (s), 3.34 (s), 3.37 (s), 3.41 (s), 3.48• (s?), 3.67 (av), 3.81 (v.w.), 3.89 (v.w.), 3.95 (v.w.), 4.15 (v.w.), 4.44 (v.w.), 4.73 (av), 5.05 (v.w.), 5.50 (s), 5.79 (av), 6.17 (s), 6.89 (s), 7.08• (s), 7.25 (s), 7.86 (s), 8.13• (s), 8.52 (w), 9.12• (av), 9.85 (s), 10.42• (av), 11.07 (s), 11.95 (s), 12.79 (v.w.), 13.13 (w), 13.88 (w) μ.

3-3-Methylpenten-1-yne. 3.03 (s), 3.22 (av), 3.29• (s), 3.35 (s), 3.40 (s), 3.48• (s), 3.51• (s), 3.67 (w), 3.82 (v.w.), 3.98 (v.w.), 4.06 (v.w.), 4.12 (v.w.), 4.18 (v.w.), 4.73 (av), 5.12 (v.w.), 5.51 (av), 6.19 (s), 6.87 (s), 7.02 (s)•, 7.24 (s), 7.46 (s), 7.81 (s), 8.15 (s), 9.22• (av), 9.43• (s), 9.60 (s), 9.92 (av), 10.04• (av), 10.98 (v.s.), 12.24 (s), 12.55• (av), 13.60 (w), 14.02 (w) μ.

3'3'-Dimetho-3-3-ethylbuten-1-yne. 3.03 (s), 3.22 (av), 3.37 (v.s.), 3.41 (s), 3.45 (s), 3.50 (s), 3.69 (w), 3.76 (v.w.), 3.92 (v.w.), 4.05 (v.w.), 4.19 (v.w.), 4.34 (v.w.), 4.51 (v.w.), 4.71 (w), 4.85• (v.w.), 5.07 (v.w.), 5.48 (av), 5.81• (v.w.), 6.06• (av), 6.21 (s), 6.35• (av), 6.74 (s), 6.80 (s), 7.20 (s), 7.31 (s), 7.86• (av), 8.25 (s), 8.54 (s), 9.31 (w), 9.70 (av), 11.01 (v.s), 12.07 (w), 13.88 (w), 14.78 (av) μ.

1-Penten-3-yne. 3.21 (s), 3.27• (s), 3.30 (s), 3.34 (s), 3.40 (s), 3.50 (s), 3.66 (av), 3.83 (v.w.), 3.91• (v.w.), 3.96 (v.w.), 4.07 (v.w.), 4.15 (v.w.), 4.43 (s), 4.53 (av), 4.82 (w), 5.10 (w), 5.40 (s), 6.04• (av), 6.22 (s), 6.92 (s), 7.05 (s), 7.25• (s), 7.72 (av), 8.53 (s), 9.35• (av), 9.72 (s), 10.25 (v.s.), 10.87 (v.s.), 11.49• (w?), 13.42 (av), 14.26 (av), 14.80 (av) μ.

1-Hexen-3-yne. 3.21 (s), 3.29• (av), 3.36 (s), 3.41 (s), 3.44• (s), 3.49• (s), 3.53• (av), 3.64 (w), 3.68 (w), 3.84 (w), 4.05 (v.w.), 4.11 (v.w.), 4.15 (v.w.), 4.43 (s), 4.52• (av), 4.73 (v.w.), 4,88 (v.w.), 5.14 (w), 5.40 (av), 6.03• (av), 6.22 (s), 6.81 (s), 6.92• (av), 7.03• (av), 7.24 (av), 7.56 (s), 8.57 (s), 9.34 (av), 9.63 (av), 10.20 (v.s.), 10.88 (v.s.), 12.82 (av) μ.

1-Hepten-3-yne. 3.21 (s), 3.25• (s?), 3.31 (s), 3.35 (v.s.), 3.41 (v.s.), 3.48 (s), 3.54 (s), 3.66 (v.w.), 3.75 (v.w.), 3.83 (v.w.), 3.97 (v.w.), 4.08 (v.w.), 4.20 (v.w.), 4.44 (s), 4.52• (w), 4.55• (w), 4.87 (v.w.), 5.12 (w), 5.48 (av), 6.10• (av), 6.22 (s), 6.85 (s), 6.94• (s), 7.03• (s), 7.31 (s), 7.48 (s), 7.84 (s), 8.15 (av), 8.62 (s), 8.94• (av), 9.14• (av), 9.31 (av), 9.57 (av), 10.21 (v.s.), 10.88 (v.s), 12.58 (av), 13.61 (av), 14.78 (av) μ.

1-Octen-3-yne. 3.22 (av), 3.31 (s), 3.37 (v.s.), 3.49 (s), 3.54• (s?), 3.67 (v.w.), 3.79 (v.w.), 3.88 (v.w.), 3.91 (v.w.), 3.94 (v.w.), 4.18 (w), 4.35• (v.w.), 4.44 (s), 4.51• (w), 4.65• (v.w.), 4.87• (v.w.), 5.13 (w), 5.46 (av), 6.08• (av), 6.22 (s), 6.85 (s), 6.94• (s), 7.03• (s), 7.24 (s), 7.31• (av), 7.54 (s), 7.72 (av), 7.99 (av), 8.23 (w), 8.62 (s), 9.03 (av), 9.49• (w), 9.73 (av), 10.27 (s), 10.90 (s), 12.07 (v.w.), 13.32 (av), 13.78 (av), 14.89 (av) μ.

1-Hexen-4-yne. 3.23 (s), 3.31 (s), 3.34 (s), 3.43 (v.s.), 3.46• (s), 3.51• (s), 3.55• (s), 3.67 (av), 3.81 (v.w.), 3.84* (v.w.), 3.92 (v.w.), 3.99 (v.w.), 4.06 (v.w.), 4.15 (v.w.), 4.31 (v.w.), 4.41 (w), 4.83 (w), 5.04 (w), 5.40 (av), 6.08 (s), 7.00 (v.s.), 7.24 (s), 7.50 (s), 7.78 (s), 8.25 (av), 8.70 (av), 8.97 (av), 9.48 (av), 10.06 (v.s.), 10.90 (v.s.), 11.88 (v.w.), 12.73 (av), 13.80 (w) μ.

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*The vinylacetylene was investigated in 10% solution in CCl_4 with a layer thickness of 0.25, 0.1 and 0.03 mm. The asterisks signify frequencies occurring as peaks on other frequencies. The intensities of the bands are as follows: v.s. = very strong, s = strong, av = average, w = weak, v.w. = very weak.

SUMMARY

1. The infrared spectra of 11 structurally different vinylacetylene hydrocarbons were investigated.

2. It was shown that the principal laws found in the infrared spectra of ethylene-, acetylene- and 1,3-diene hydrocarbons are also observed in the present case.

3. It was established that in hydrocarbons of this type the vinyl group is characterized by frequencies of 3110, 3030, 1608, 1420, 975, 920 cm^{-1}, the $-CH{=}CH-$ (trans) group by frequencies of 3040, 1620, 955 cm^{-1}, the $CH_2{=}C-$ group by frequencies of 3105, 1620, 1410, 905 cm^{-1}, the terminal acetylene group by frequencies of 3300, 2115, the same group in the middle of the molecule by a frequency of about 2250 cm^{-1}. Conjugation causes displacement of the absorption bands of the multiple bonds into the long-wave region.

4. It was shown that the intensities of the absorption bands corresponding to multiple bonds are in conformity with the supposed migration of the electrons in a conjugated system under the influence of radicals.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

LXXV. THE INTERACTION OF PROPARGYL BROMIDE WITH ALIPHATIC ALDEHYDES UNDER THE CONDITIONS OF THE REFORMATSKY REACTION

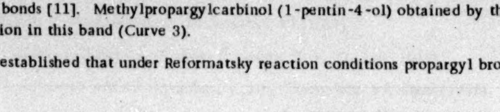
A.A. Petrov, Yu.I. Porfiryeva and G.I. Semenov

In recent literature considerable attention has been paid to acetylene-allene rearrangements during the process of chemical conversions of acetylene haloid derivatives of the propargyl type [1-7]. The experimental data accumulated indicate that the way in which the propargyl halides are converted depends on their structure and the nature of the reagents. Instances are known in which exchange reactions with participation of these conversions are not accompanied by isomerization; in the majority of cases, however, mixtures of allene and acetylene compounds are obtained.

According to data in the literature [8], only acetylene alcohols – alkylpropargylcarbinols – are formed in reactions of propargyl bromide with zinc and carbonyl compounds. We required these alcohols as initial substances for the synthesis of alkylacetylenes. We carried out several experiments on the condensation of propargyl bromide with acetic and propionic aldehydes under Reformatsky reaction conditions and obtained two alcohols (C_5H_7OH and C_6H_9OH), the first of which was assumed to be 1-pentin-4-ol and the second 1-hexin-4-ol. We also obtained 1-pentin-4-ol by the action of propylene oxide on sodium acetylide in liquid ammonia. It had also been obtained by this method previously [9, 10].

The constants of both samples of the alcohol C_5H_7OH (from propargyl bromide and sodium acetylide) show little difference from each other. The molecular refraction for both alcohols agreed well with that calculated allowing for the presence of only a triple bond in the compound. The same was also noted for the alcohol C_6H_9OH (from propionic aldehyde). In the meantime infrared spectra of alcohols obtained by the first method indicated that they contain a considerable admixture of allene alcohols (Figure 1, Curves 1 and 2). As well as absorption bands of 3300 and 2130 cm^{-1}, characteristic of compounds with a terminal acetylene group, the spectra of these alcohols included an intensive absorption band of 1960 cm^{-1}, which is only found in compounds containing an allene system of multiple bonds [11]. Methylpropargylcarbinol (1-pentin-4-ol) obtained by the second method shows very weak absorption in this band (Curve 3).

It was, therefore, established that under Reformatsky reaction conditions propargyl bromide reacts in two ways.



$$R\text{—}CHO + Zn + CH_2Br\text{—}C{\equiv}CH\text{—}\begin{cases} \rightarrow R\text{—}CHOH\text{—}CH_2\text{—}C{\equiv}CH \quad (I) \\ \rightarrow R\text{—}CHOH\text{—}CH{=}C{=}CH_2 \quad (II) \end{cases}$$

There is undoubtedly a predominance of acetylene alcohols in the reaction products but exact data on their content can only be obtained when it is possible to separate the allene alcohols in a pure state.

It is interesting to note that as a result of the dehydration of both the alcohols obtained from propargyl bromide (by Eglinton and Whitehead's method [12] via the esters of p-toluene sulfonic acid) vinylacetylene hydrocarbons are formed without any appreciable admixture of allene compounds. In the region of about 1950 cm^{-1} these hydrocarbons have only very weak absorption bands which are found in the case of all dienes and vinylacetylenes with conjugated multiple bonds (Curves 4 and 5). At the same time both hydrocarbons have intensive

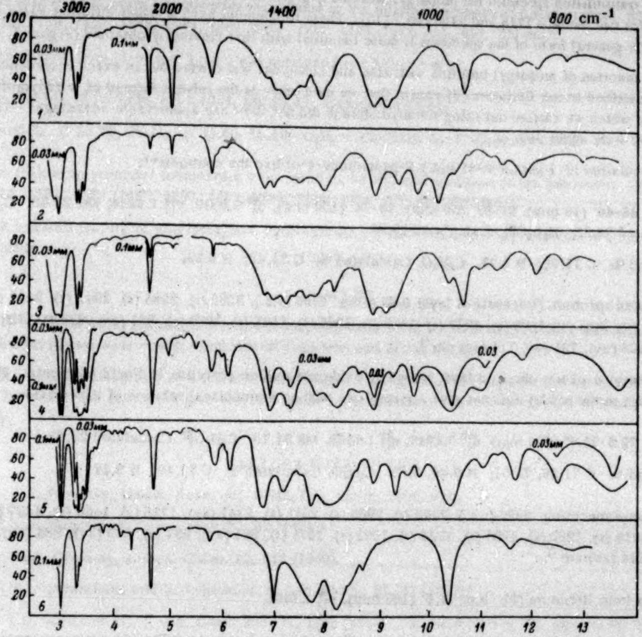


Fig. 1. The infrared spectra of alcohols and hydrocarbons: 1) alcohol from propargyl bromide and acetaldehyde; 2) alcohol from propargyl bromide and propionic aldehyde; 3) alcohol from sodium acetylide and propylene oxide (1-pentin-4-ol); 4) 3-penten-1-yne; 5) 3-hexen-1-yne; 6) propargyl bromide.

frequencies, characteristic of the ethylene (1623 cm^{-1}) and acetylene (3300 and 2110 cm^{-1}) groups. Isomeric acetylene and allene alcohols of this type evidently split off the sulfonic acid units to form vinylacetylene hydrocarbons, similar to the way in which 4-chloro-1,2-butadiene gives vinylacetylene as a result of dehalogenation [13].

EXPERIMENTAL

Commercial grades of acetaldehyde and propionic aldehyde were used. They were first distilled, using a Widmer column. The propargyl bromide was obtained from propargyl alcohol by the action of phosphorus tribromide in pyridine [14].

B.p. 82-83°, d_4^{20} 1.5823, n_D^{20} 1.4915. Data from literature [14]: b.p. 82°, d^{19} 1.579, n_D^{20} 1.4942.

Infrared spectrum*: 3289 (s), 3021 (s), 2950 (s), 2882 (v.w.), 2825 (v.w.), 2625 (w), 2558 (v.w.), 2506 (v.w.), 2410 (w), 2294 (w), 2188 (v.w.), 2141 (av), 2092 (v.w.), 2028 (w), 1730 (w), 1615 (v.w.), 1424 (s), 1289 (s), 1212 (s), 1181 (av), 1105 (w), 1042 (w), 962 (s), 861 (w), 781 (w), 692 (av).

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*The infrared spectra were taken on an IKS-2 biradiant spectrograph employing an LiF prism for the 3-5μ range and an NaCl prism for the 5-15μ range. The authors wish to express their gratitude to M.S. Barvinok for permission to use the spectrograph.

The transmission spectrum for propargyl bromide is given in the literature but numerical data are only available for two bands – 1715 and 2105 cm^{-1} [15]. These frequencies have a rather different value in our case although the general form of the spectrum is quite identical with that previously obtained (Figure 1, Curve 6).•

The reaction of propargyl bromide with zinc and aldehydes was carried out in exact accordance with the method prescribed in the literature [8] except that we used ether as the solvent instead of tetrahydrofurane. An experiment which we carried out using tetrahydrofurane did not show any appreciable advantages. The yields of the alcohols were about 50%.

The mixture of 1-pentin-4-ol and 1,2-pentadiene-4-ol had the constants••:

B.p. 45-46° (10 mm), 61-62° (50 mm), 75-76° (100 mm), d_4^{20} 0.9039, n_D^{20} 1.4384, MR 24.46. $C_5H_8O|\equiv$. Calculated 24.81. $C_5H_8O|=_2$. Calculated 25.88.

Found %: C 71.01; H 9.73. C_5H_8O. Calculated %: C 71.40; H 9.59.

Infrared spectrum (thickness of layer 0.03 mm): 3390 (v.s.), 3289 (s), 2985 (s), 2941 (s), 2141 (av), 1965 (av), 1715 (s), 1451 (s), 1427 (s), 1377 (s), 1350 (s), 1266 (s), 1121 (s), 1089 (s), 961 (av), 937 (s), 925 (w), 883 (w), 853 (av), 828 (av), 791 (w), 714 (av) cm^{-1}.

1-Pentin-4-ol was obtained from propylene oxide and sodium acetylide in liquid ammonia. The 30% yield (with respect to the oxide) does not give a precipitate with an ammoniacal solution of silver oxide.

B.p. 72.5-73.5° (100 mm), d_4^{20} 0.8918, n_D^{20} 1.4368, MR 24.70. $C_5H_8O|\equiv$. Calculated 24.81.

Found %: C 71.38, 71.51; H 9.40, 9.50. C_5H_8O. Calculated %: C 71.40; H 9.59.

Infrared spectrum: 3390 (v.s.), 3300 (s), 2985 (s), 2941 (s), 2141 (av), 1715 (s), 1456 (s), 1427 (s), 1379 (s), 1350 (s), 1316 (s), 1282 (s), 1225 (s), 1124 (s), 1092 (s), 1075 (s), 961 (av), 937 (s), 909 (av), 883 (av), 827 (av), 791 (av), 714 (av) cm^{-1}.

Data from literature [9]: b.p. 74.6° (100 mm), n_D^{16} 1.4406.

1-Hexin-4-ol with an admixture of 1,2-hexadiene-4-ol and with the following constants was obtained from propargyl bromide and propargyl aldehyde under the same conditions:

B.p. 54-55° (20 mm), 71-72° (50 mm), d_4^{20} 0.8958, n_D^{20} 1.445, MR 29.13. $C_6H_{10}O|\equiv$. Calculated 29.43. $C_6H_{10}O|=_2$. Calculated 30.60.

Found %: C 72.92; H 10.35. $C_6H_{10}O$. Calculated %: C 73.43; H 10.27.

A precipitate is not formed with an ammoniacal solution of silver oxide.

Hydrocarbons were obtained from both the alcohols. The alcohols were converted by the action of p-toluenesulfonyl chloride in pyridine into p-toluenesulfonic acid esters and the latter were distilled with aqueous alkali with the addition of Petrov's contact.••• The yield of the p-toluene sulfonic esters was of the order of 80-90%, that of the hydrocarbons 70-75%.

Propenylacetylene (3-penten-1-yne) was obtained from 1-pentyl-4-ol.

B.p. 46.5-47.5°, d_4^{20} 0.7293, n_D^{20} 1.4348, MR 23.64. $C_5H_6|=|\equiv$. Calculated 22.82. Data from literature [12]: b.p. 46-48°, n_D^{19} 1.4356.

•The value of the frequencies we obtained for the acetylene bond in propargyl bromide may be taken as more reliable because all the investigated alkylacetylenes have absorption bands in the 2135-2150 cm^{-1} range [11].

••In different experiments, samples of this alcohol, distinguished from each other somewhat as regards specific gravity and refractive index, were obtained.

•••According to data in the literature Teepol [12] should be added.

The following principal frequencies were found in the infrared spectrum of the substance: 3300, 3049, 2983, 2114, 1718, 1623, 1445, 1383, 1360, 1280, 1221, 1119, 1029, 955, 843, 729 cm^{-1}.

Butenylacetylene (3-hexen-1-yne) was obtained from 1-hexin-4-ol.

B.p. 72-74°, d_4^{20} 0.7425, n_D^{20} 1.4381, MR 28.33; Calculated 27.44.

Found % C 89.79, 90.11; H 10.60, 10.49. C_6H_8. Calculated % C 89.94; H 10.06.

The following principal frequencies were found in the infrared spectrum of the substance: 3300, 3040, 2976, 2114, 1701, 1623, 1468, 1393, 1299, 1234, 1119, 1070, 955, 853, 736 cm^{-1}.

The infrared spectra of vinylacetylene hydrocarbons are considered in detail in another communication of our laboratory.

SUMMARY

1. It was shown that propargyl bromide reacts with acetic and propionic aldehydes under Reformatsky reaction conditions in two ways – with formation of acetylene and allene alcohols.

2. It was established that as a result of dehydration (via the esters of p-toluenesulfonic acid) the alcohols obtained from both the aldehydes give vinylacetylene hydrocarbons – 3-penten-1-yne and 3-hexen-1-yne, respectively.

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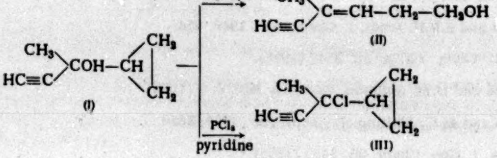
THE MECHANISM OF THE CONVERSIONS OF TERTIARY ALCOHOLS OF THE CYCLOPROPANE SERIES UNDER THE INFLUENCE OF MINERAL AND ORGANIC ACIDS

VI. THE REACTION OF METHYLETHYNYLCYCLOPROPYLCARBINOL WITH SULFURIC ACID AND WITH PHOSPHORUS TRICHLORIDE IN THE PRESENCE OF PYRIDINE. THE SYNTHESIS OF METHYLTRICHLOROMETHYLCYCLOPROPYLCARBINOL AND THE INVESTIGATION OF ITS REACTIONS WITH SULFURIC ACID

T.A. Favorskaya and L.S. Bresler

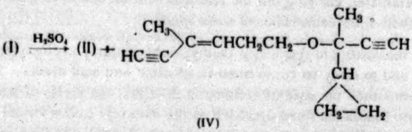
It is known that tertiary alcohols of the cyclopropane series in acid medium undergo an unusual allyl rearrangement, forming unsaturated alcohols [1], halides [2], and esters [3]. The unsaturated primary alcohols produced under these conditions are partially isomerized further to derivatives of tetrahydrofuran. The latter isomerization has been observed in all the alcohols studied which contain aliphatic radicals. It proceeds very readily upon distillation of the unsaturated alcohols with traces of acid, but for an alcohol with an aromatic radical – 2-phenylpenten-2-ol-5 – considerably more severe conditions are required for the isomerization to be accomplished [4]. Such stability of this alcohol can be explained by the presence in its molecule of a conjugated system of double bonds.

In this connection it was of interest to investigate the behavior upon treatment with sulfuric acid of methylethynylcyclopropylcarbinol, from which there should be formed by allyl rearrangement an alcohol containing in its molecule conjugated double and triple bonds.



By reaction of this alcohol with phosphorus trichloride in the presence of pyridine it could be expected that the cyclic chloride (III) would be obtained as the main reaction product. In this case it seemed that the splitting out of hydrogen chloride which has been observed in carrying out this reaction with methylisopropyl- and methyl-n-butylcyclopropylcarbinols [5], with the formation of the corresponding unsaturated cyclic hydrocarbons, need not be feared, since a cyclic chloride was obtained by the action of phosphorus trichloride and pyridine on dimethylcyclopropylcarbinol and splitting out of hydrogen chloride at the expense of the hydrogen of the methyl group has not been observed.

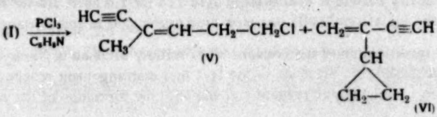
Study of the reaction of methylethynylcyclopropylcarbinol with sulfuric acid showed that in this case the reaction goes very energetically. When this reaction was carried out under the conditions used with all the alcohols that contained aliphatic radicals instead of the acetylene group (H_2SO_4 1 : 10 and boiling for an hour), complete resinification of the reaction products occurred. The best results were obtained by stirring the alcohol (I) for a half-hour with sulfuric acid 1 : 10 that was still warm after dilution. When more dilute acid was used, the reaction did not go. As a result, the primary enyne alcohol (II) and the ether of this alcohol and methylethynylcyclopropylcarbinol (IV) were obtained.


(IV)

The structure of the enyne alcohol was demonstrated by ozonizing it, which produced formic acid, acrolein, and pyruvic acid; the two latter products were identified as the 2,4-dinitrophenylhydrazones. The acrolein was formed upon distilling off the neutral materials from the aqueous solution of the products of ozonolysis, as a result of dehydration of β-hydroxypropionaldehyde. The presence of a final $\equiv$CH group was proved by the qualitative reactions of the acetylenic hydrogen. By these reactions the presence of a free acetylenic hydrogen was also demonstrated in the molecule of the ether that was obtained. For evidence of its structure, the ether was ozonized, whereupon addition was observed of 107.8% of the amount of ozone calculated for a compound with one double bond and two triple bonds, which are contained in the molecule of the primary-tertiary ether obtained.

If the ether were diprimary, it would contain two double and two triple bonds, and if it were ditertiary, it would contain only two triple bonds. Analysis of the ozonization products was not carried out, since aside from formic acid, which might be produced by the ozonization of all three ethers, it might be difficult to isolate any readily identifiable products, the more so because the quantity of ether obtained was small. The formula for the primary-tertiary ether was adopted by us because the molecular refraction found corresponded to that formula and was less than the value calculated for the diprimary ether, while in the latter case a greater exaltation should have been observed. The formula for the ditertiary ether was in general not very likely, since such ethers are almost unknown and attempts to synthesize them usually have been unsuccessful. However, it was impossible to be certain that the diprimary ether was completely absent in the product obtained by us.

The reaction of methylethynylcyclopropylcarbinol with phosphorus trichloride in the presence of pyridine goes very easily, but in this case, as also for the methyl-n-butyl- and methylisopropylcyclopropylcarbinol [5], it was not possible to obtain the cyclic chloride, but an isomerization product of it was isolated – an unsaturated primary chloride, the constants of which agreed with those of the chloride obtained earlier [6] from methylethynylcyclopropylcarbinol by the action of hydrochloric acid. Besides the chloride (V), a hydrocarbon was obtained which gave the qualitative reactions for an acetylenic hydrogen and corresponded in refraction, molecular weight, and analysis to α-cyclopropylvinylacetylene (VI). For proof of the structure of the hydrocarbon it was oxidized with potassium permanganate, yielding cyclopropanecarboxylic acid.

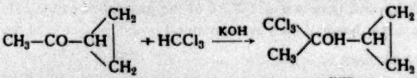

(V) (VI)

Thus, in this case also the chloride first formed on the one hand underwent an isomerization, and on the other hand split out a molecule of hydrogen chloride and formed α-cyclopropylvinylacetylene which was not previously known.

The mechanism of the isomeric conversions of trichloro alcohols in alkaline medium was worked out in detail by A.E. Favorsky [7] in the instance of the alcohols obtained by him by the action of alkali on a mixture of chloroform with acetone and with methyl propyl ketone. The production of acids of the acrylic series made this reaction very interesting; however, its further development was hindered by the low yields of the products obtained by the action of chloroform and alkali on other ketones. Since the work of A.E. Favorsky many investigators have studied the conditions for the synthesis of trichloro alcohols in the absence and in the presence of solvents, attempting in vain to obtain good yields of these compounds, and only in recent years have Weizmann et al. [8] secured good results by carrying out the reaction in methylal solution. Lombard and Boesch [9] somewhat modified the method of Weizmann, carrying out the reaction with an excess of chloroform. Since the time of A.E. Favorsky no one has studied the conversions of these alcohols.

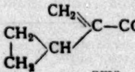
It seemed to us very interesting to synthesize methyltrichloromethylcyclopropylcarbinol from acetyltrimethylene and chloroform and to study its conversions in alkaline and acid media. It is true that good yields were not to be expected here, since the data of Weizmann show that the yields of trichloro alcohols diminish with an increase in the steric hindrance to an approach to the carbonyl carbon in the ketone molecule, and actually methyltrichloromethylcyclopropylcarbinol was obtained in 3.6% yield. The reduction in the yield was further contributed to by the circumstance that the alcohol (VII) obtained was contaminated by an admixture of unsaturated material from which it could be purified only by oxidation with potassium permanganate solution.

When the condensation was carried out by the method of Weizmann, we isolated from the reaction products an acid with m.p. 68-70°, which contained neither chlorine nor unsaturated bonds and which agreed in neutralization equivalent and elementary analysis with the formula for α-cyclopropyl-α-hydroxypropionic acid (X).

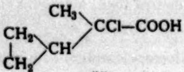


(VII)

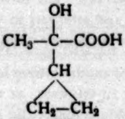
Upon conversion of the alcohol (VII) in alkaline medium we might expect, according to the mechanism of A.E. Favorsky, the formation of cyclopropylacrylic acid (VIII), α-chloro-α-cyclopropylpropionic acid (IX), and α-hydroxy-α-cyclopropylpropionic acid (X).



(VIII)



(IX)

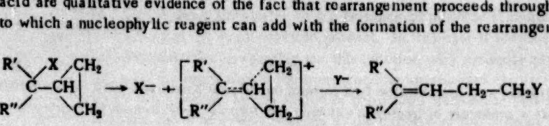


(X)

Of all these acids, we found only acid (X).

By the action of sulfuric acid on methyltrichloromethylcyclopropylcarbinol we might expect to produce the unsaturated alcohol 2-trichloromethylpenten-2-ol-5; however, neither by boiling alcohol (VII) with sulfuric acid 1 : 10 for 4.5 hours nor by boiling it with sulfuric acid 1 : 5 for 1.5 hours did we succeed in separating any isomerization product, and the alcohol (VII) was recovered unchanged in both instances.

The results of the investigation of the conversions of tertiary alcohols of the cyclopropane series in the presence of sulfuric acid are qualitative evidence of the fact that rearrangement proceeds through the formation of a carbonium ion to which a nucleophylic reagent can add with the formation of the rearrangement product.



Formation of the carbonium ion is probable for the tertiary derivatives, the more so since in the case in question the carbonium ion is stabilized by conjunction with the cyclopropyl radical. Methylethynylcyclopropylcarbinol is isomerized by a half-hour's stirring with sulfuric acid solution in the cold, while prolonged boiling with H_2SO_4 solution is necessary for the rearrangement of dimethyl- and methylethylcyclopropylcarbinol. The acetylenic radical additionally stabilizes the cation as a result of conjugation. On the other hand, a cation is not formed from methyltrichloromethylcyclopropylcarbinol and rearrangement does not take place, since the CCl_3 group exerts a large negative inductive effect.

EXPERIMENTAL

Methylethynylcyclopropylcarbinol (I) was prepared by the condensation of acetyltrimethylene with acetylene in the presence of powdered potassium hydroxide by the method of A.E. Favorsky, adapted to the case in question by A.P. Golovchanskaya [10]. The yield of alcohol was 80%.

Reaction of methylethynylcyclopropylcarbinol with sulfuric acid. To 25.8 g of methylethynylcyclopropylcarbinol was added 110 ml of sulfuric acid 1 : 10, which was at a temperature of 30-40°. After stirring for a half-hour, the oily layer was separated and the aqueous layer was extracted with ether. After washing with sodium carbonate solution and drying with calcined sodium sulfate, the ether was distilled off and the residue was distilled in vacuo. Two fractions were obtained: 1st with b.p. 72-74° (4 mm), 6.9 g (26.8%); 2nd with b.p. 103-104° (4 mm), 6.8 g (28.7%). A considerable amount of tar remained in the distilling flask. Both fractions gave a white, acid-soluble precipitate with an ammoniacal solution of silver oxide, and a yellow precipitate with the copper reagent of Ilosvei. The 1st fraction reacted with methylmagnesium iodide, the 2nd did not. The 1st fraction was the primary alcohol 3-methylhexen-3-yn-1-ol-6, and the 2nd was the ether of this alcohol and methylethynylcyclopropylcarbinol (IV). Both substances were colorless liquids with a pleasant odor, turning yellow upon standing even in sealed ampoules.

3-Methylhexen-3-yn-1-ol-6. B.p. 72-74° (4 mm), 104-105° (37 mm), n_D^{20} 1.4847, d_4^{20} 0.9174, MR_D 34.40. $C_7H_{10}O|^{=}|^{\equiv}$. Calculated 33.48.

Found %: C 76.57; H 9.55; OH 16.18. M 110.7. $C_7H_{10}O$. Calculated %: C 76.32; H 9.15; OH 15.44. M 110.2.

Ether. B.p. 103-104° (4 mm), 138-139° (38 mm), n_D^{20} 1.4821, d_4^{20} 0.9190, MR_D 62.76. $C_{14}H_{18}O|^{\equiv}_2|^{=}\Delta$. Calculated: 62.33. $C_{14}H_{18}O|^{=}_2|^{\equiv}_3$. Calculated 63.36.

Found %: C 83.11; H 9.28. M 195.8. $C_{14}H_{18}O$. Calculated %: C 83.12; H 8.97. M 202.3.

Upon ozonization of 3.2 g of alcohol (II), 2.67 g of ozone (95.6% of theoretical) was taken up. The ozonide was decomposed with water and in a portion of the solution formic acid was determined by the method of Fincke [11] (yield 77.3%). The remaining solution was neutralized with sodium carbonate and the neutral products were steam distilled into a solution of 2,4-dinitrophenylhydrazine. The melting point of the dark red crystals obtained was 162-163° (from methyl alcohol) [12] in a sealed capillary. A mixed sample with the 2,4-dinitrophenylhydrazone of known acrolein gave no depression.

The acid salts were concentrated to a small volume and carefully acidified with concentrated hydrochloric acid. Pyruvic acid was determined by the method of Neuberg and Kobel [13] as the 2,4-dinitrophenylhydrazone, m.p. 214-215° (from glacial acetic acid) [14]. A mixed sample with the 2,4-dinitrophenylhydrazone of known pyruvic acid gave no depression.

For the ozonization of the ether, 1.7 g of material was taken. 1.29 g of ozone was absorbed (107.8% of the theoretical amount for $C_{14}H_{18}O|^{=}|^{\equiv}_2$). The products of ozonolysis were not analyzed.

Reaction of methylethynylcyclopropylcarbinol with phosphorus trichloride in the presence of pyridine was carried out under the same conditions as in the case of dimethylcyclopropylcarbinol [6]: 1/3 mole of phosphorus trichloride and 1/3 mole of pyridine was taken to 1 mole of the alcohol. To 10.0 ml of phosphorus trichloride there was added over a period of an hour and a half, while stirring and cooling with ice, 36.9 g of methylethynylcyclopropylcarbinol mixed with 8.9 g of pyridine, after which stirring and cooling were continued for an hour more. Then the solution was decanted from the precipitate of phosphorus acid that had separated, dried with calcined magnesium sulfate, and distilled. Two fractions were obtained upon distillation.

1st fraction amounting to 3.4 g [11% calcined on the basis of the hydrocarbon (VI)] – colorless, very volatile substance with a pungent, unpleasant odor. Positive qualitative reaction for an acetylenic hydrocarbon, contained no halogen; according to the analytical data it was cyclopropylvinylacetylene (VI).

B.p. 98-102°, d_4^{20} 0.8626, n_D^{20} 1.4702, MR_D 29.81. $C_7H_8\Gamma\digamma\Delta$ Calculated 30.42.

Found %: C 91.14; H 8.94. M 102. C_7H_8. Calculated %: C 91.25; H 8.75. M 92.

2nd fraction, 3.9 g [calculated on the basis of the primary chloride (V)], contained an acetylenic hydrocarbon and gave a positive test for halogen (Beilstein). The substance was 3-methyl-6-chlorohexen-3-yne-1 (V).

B.p. 106-107° (150 mm), d_4^{20} 0.9655, n_D^{20} 1.4800.

Literature data [6]: d_4^{20} 0.9657, n_D^{20} 1.4799.

The structure of the hydrocarbon (VI) was confirmed by oxidation. 0.5 g of the hydrocarbon required 4.1 g of potassium permanganate. The manganese dioxide was filtered off and washed with hot water. The filtrate was concentrated to dryness on the water bath and the salts of the organic acids were extracted by boiling with anhydrous alcohol. The alcohol was distilled off, the salts were decomposed with sulfuric acid 1 : 5, and the acids were extracted with ether. A current of dry ammonia was passed into the ethereal solution, which had been dried over calcined magnesium sulfate, and the ammonium salt that precipitated was filtered off and dried in a vacuum desiccator over calcium chloride. M.p. 104-104.5°. According to the data in the literature [15], the salt of cyclopropanecarboxylic acid melts at 115°. The ammonium salt was converted to the silver salt and dried in a vacuum desiccator over sulfuric acid.

Found %: Ag 56.18. $C_4H_5O_2Ag$. Calculated %: Ag 55.98.

Methyltrichloromethylcyclopropylcarbinol (VII) was prepared by the condensation of acetyltrimethylene with anhydrous chloroform in the presence of powdered potassium hydroxide in anhydrous methylal medium according to the method of Weizmann [8] or by the modified method of Lombard [9]. The chloroform, as in the work by Lombard, was dried with calcined calcium chloride and distilled over phosphoric anhydride. The methylal was prepared by the method of Fischer and Gieber [16]. The crude methylal was dried over calcined lime, distilled on a column, and then over metallic sodium.

The condensation of acetyltrimethylene with chloroform by the method of Weizmann was carried out in the following manner. 125 ml of anhydrous methylal was placed in a three-necked flask fitted with a stirrer, thermometer, and reflux condenser, and was cooled to −5° (ice and salt), after which 30 g of technical, powdered potassium hydroxide was added. After stirring for a half-hour, we began to carefully drop in a mixture of 53.7 g of $CHCl_3$ and 42 g of acetyltrimethylene at such a rate that the reaction temperature did not rise above −1°. The addition extended over 2 hours, after which stirring was continued for another 2 hours. There was considerable formation of tar. After decomposition with ice water and 30% H_2SO_4 and appropriate working up of the reaction products, we isolated 12.5 g of unreacted acetyltrimethylene and 2.1 g (2.1%) of the trichloro alcohol (VII) with b.p. 84-87° (10 mm), contaminated with unsaturated material. From the acid aqueous solution that remained after steam distillation of the neutral products, a crystalline acid was isolated in the amount of 0.1 g with m.p. 68-70°, which was, according to the analytical data, α-hydroxy-α-cyclopropylpropionic acid (X).

Found %: C 55.15; H 7.81. Equiv.141. $C_6H_{10}O_3$. Calculated %: C 55.37; H 7.75. Equiv. 130.

When the reaction was carried out according to the procedure of Lombard, the ketone and the chloroform were added in succession, and not simultaneously, and twice the amount of chloroform was used. With this procedure tar formation was almost unnoticeable. The yield of the trichloro alcohol in this case was 3.7 g (3.6%), and much of the acetyltrimethylene was recovered. No acid reaction products were isolated. The methyltrichloromethylcyclopropylcarbinol (VII) was freed of unsaturated contaminant by treatment with potassium permanganate solution.

B.p. 90-92° (13 mm), n_D^{20} 1.4985, d_4^{20} 1.3428, MR_D 44.43; Calculated 44.54.

Found %: Cl 52.02; OH 8.22. $C_6H_9OCl_3$. Calculated %: Cl 52.27; OH 8.35.

Reaction of methyltrichloromethylcyclopropylcarbinol (VII) with sulfuric acid. 4 g of the alcohol was boiled with 55 ml of sulfuric acid 1:10 for 4.5 hours. The heavy, oily layer became yellow, was extracted with ether, and the extract was washed with sodium carbonate solution and dried with $MgSO_4$. After the solvent was distilled off and the product was distilled, 2.1 g of the starting alcohol was obtained with b.p. 86-87° (14 mm), n_D^{20} 1.4995.

2.1 g of the alcohol was boiled for 1.5 hours with 30 ml of H_2SO_4 1:5. After appropriate treatment, 0.6 g of the starting alcohol was isolated.

B.p. 110° (30 mm), n_D^{20} 1.5002.

Found %: OH 7.92. $C_6H_8Cl_3OH$. Calculated %: OH 8.35.

SUMMARY

1. The reaction of methylethynylcyclopropylcarbinol with sulfuric acid has been investigated. It has been shown that this conversion proceeds very easily, with the formation of a primary enyne alcohol, 3-methylhexen-3-yn-1-ol-6, and the ether of this alcohol with the starting cyclic alcohol.

2. In the investigation of the reaction of methylethynylcyclopropylcarbinol with phosphorus trichloride in the presence of pyridine, the products were α-cyclopropylvinylacetylene and the enyne chloride 3-methyl-6-chlorohexen-3-yne-1.

3. Methyltrichloromethylcyclopropylcarbinol has been synthesized for the first time and it has been shown that this alcohol is not altered by heating with solutions of sulfuric acid of different concentrations.

4. On the basis of the data obtained, it has been suggested that the rearrangement of tertiary alcohols of the cyclopropane series in the presence of sulfuric acid proceeds through the formation of a carbonium ion, which by recombination gives the rearrangement product.

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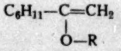
REACTION OF CYCLOHEXYLACETYLENE WITH THE LOWER SATURATED MONOBASIC ACIDS

A.I. Bolshukhin and A.G. Egorov

In our earlier papers [1], we have described the addition of acetic, propionic, and butyric acids to octyne-1 and its isomers 3-methyl-3-ethylpentyne-1 and 3,3-dimethylhexyne-1, leading to the formation of the appropriate vinyl β-esters and the corresponding ketones.

In the present investigation we have studied the reaction of these same acids in the presence of their mercury salts and boron fluoride etherate with cyclohexylacetylene.

We have isolated 1-acetoxy-1-cyclohexylethene (I), 1-propionoxy-1-cyclohexylethene (II), 1-butyroxy-1-cyclohexylethene (III), and in all cases methyl cyclohexyl ketone.



$$\begin{array}{l} C_6H_{11}\text{—}\underset{\displaystyle \overset{|}{O}\text{—}R}{C}\text{=}CH_2 \end{array}$$

(I) $R = COCH_3$, (II) $R = COC_2H_5$, (III) $R = COC_3H_7$

All of the esters described by us were colorless, transparent, mobile liquids, having an odor reminiscent of methyl cyclohexyl ketone. All of them were hydrolyzed at 100-110° in the presence of acetic acid-semicarbazide considerably more slowly than the esters previously described by us [1]. A reduced reactivity is characteristic of substances having a cyclohexyl radical in the molecule [2]. In all cases we found among the hydrolysis products only methyl cyclohexyl ketone, which confirms the correctness of the formulas (I), (II), and (III) written for the esters.

EXPERIMENTAL

The starting material, 1,1-dichloro-2-cyclohexylethane was prepared by us by the condensation of vinyl chloride with cyclohexyl chloride by the method of L. Schmerling [3]. Yield 37.7% based on the cyclohexyl chloride entering into the reaction: b.p. 92-95° (11 mm), n_D^{20} 1.4811.

Cyclohexylacetylene. 21 g of dry potassium hydroxide and 23 g of 1,1-dichloro-2-cyclohexylethane were heated with continuous stirring and the reaction products were distilled off. The distillate (b.p. 100-133°) was diluted with ether and dried with fused calcium chloride. 5.9 g (47%) of cyclohexylacetylene and 2.4 g of unreacted starting dichloride were obtained.

B.p. 129.5-132°, d_0^0 0.8727, d_{20}^{20} 0.8556, d_4^{20} 0.8543, n_D^{20} 1.4580, MR_D 34.56; calculated 34.94.

1-Acetoxy-1-cyclohexylethane. 2.6 g of acetic anhydride, 26 g of glacial acetic acid, and 1.4 g of mercuric oxide were heated until the latter dissolved. To the cooled reaction mixture was added 1 ml of boron fluoride etherate (b.p. 124-126°) and 40 g of cyclohexylacetylene (b.p. 129.5-132°). The reaction was completed in an hour and was accompanied by strong evolution of heat. The cooled reaction mixture was diluted with ether, washed with water and then with sodium carbonate solution, and dried with calcium chloride. 21 g (33.8%) of 1-acetoxy-1-cyclohexylethane was obtained.

B.p. 123.5-124.5° (56 mm), d_0^0 0.9900, d_{20}^{20} 0.9742, d_4^{20} 0.9725, n_D^{20} 1.4582, MR_D 47.22. $C_{10}H_{16}O_2$F. Calculated 47.37.

Found %: C 71.29, 71.28; H 9.59, 9.61. M 166, 163. $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.59. M 168.

As by-products there appeared 4.0 g of high-molecular substances, which were not investigated, and [illegible].2 g of methyl cyclohexyl ketone. The amount of the latter was determined by isolation of the semicarbazone with m.p. 174-175° (from alcohol) (mixed m.p. test).

Reaction of 1-acetoxy-1-cyclohexylethane with acetic acid-semicarbazide. 1.24 g of 1-acetoxy-1-cyclohexylethane (b.p. 123.5-124.5° at 56 mm) was dissolved in 22-23 ml of acetic acid-semicarbazide solution prepared as previously described [1]. After shaking the reaction mixture, it was held at 100-110° for an hour and 30 minutes. 0.95 g (70%) of semicarbazone with m.p. 174-175° (from alcohol) was obtained, which gave no lowering of melting point when mixed with an equal amount of the known semicarbazone of methyl cyclohexyl ketone.

1-Propionoxy-1-cyclohexylethane. 27.4 g of propionic acid (b.p. 139-141°, n_D^{20} 1.3860) and 1.7 g of mercuric oxide were heated until the latter was fully dissolved. To the cooled reaction mixture were added 1 ml of boron fluoride etherate $BF_3 \cdot O(C_2H_5)_2$ and 40 g of cyclohexylacetylene (b.p. 129.5°). The reaction weakly evolved heat. The reaction was completed in 1 hour, but stirring was continued for 2 hours more. The reaction products were diluted with ether, washed with water and with sodium carbonate solution, and dried with calcium chloride. 12.1 g (18%) of 1-propionoxy-1-cyclohexylethane was obtained.

B.p. 94.5-96° (6 mm), d_0^0 0.9748, d_{20}^{20} 0.9601, d_4^{20} 0.9585, n_D^{20} 1.4580, MR_D 51.88. $C_{11}H_{18}O_2\vDash$. Calculated 51.99.

Found %: C 72.20, 72.20; H 10.20, 9.96. M 176, 181. $C_{11}H_{18}O_2$. Calculated %: C 72.48; H 9.96. M 182.

Investigation of the fractions of the products of the synthesis showed that 9.5 g of the starting hydrocarbon (25%) was converted into high-molecular substances and approximately 10 g went into the formation of methyl cyclohexyl ketone. The latter was verified by isolation from the intermediate fractions of a semicarbazone with m.p. 173-175° (from alcohol), which gave no depression in melting point when mixed with an equal amount of known semicarbazone of methyl cyclohexyl ketone.

By the reaction of 1-propionoxy-1-cyclohexylethane with acetic acid-semicarbazide under the conditions described for the preceding experiment, there was obtained from 1.1 g of 1-propionoxy-1-cyclohexylethane 0.53g (47.6%) of the semicarbazone of methyl cyclohexyl ketone with m.p. 173-175° (from alcohol) (mixed m.p. test).

1-Butyroxy-1-cyclohexylethane. 32.5 g of butyric acid (b.p. 161-163°) and 1.7 g of mercuric oxide were heated until the latter dissolved. To the cooled reaction mixture were added 1 ml of boron fluoride etherate and 40 g of cyclohexylacetylene (b.p. 129.5°). The reaction proceeded under the same conditions as in the preceding experiment and was completed in 1 hour, but stirring was continued at room temperature for 2 hours more. After the usual further treatment of the reaction products, 22.0 g (30%) of 1-butyroxy-1-cyclohexylethane was obtained.

B.p. 96-98° (5 mm), d_0^0 0.9639, d_{20}^{20} 0.9487, d_4^{20} 0.9472, n_D^{20} 1.4560, MR_D 56.34. $C_{12}H_{20}O_2\vDash$. Calculated 56.59.

Found %: C 73.51, 73.42; H 10.31, 10.30. M 192, 194. $C_{12}H_{20}O_2$. Calculated %: C 73.43; H 10.27. M 196.

Investigation of the fractions showed that 11 g of the starting hydrocarbon was converted into high-molecular compounds, which were not studied, 3.8 g went into the formation of methyl cyclohexyl ketone, and 12 g into ester formation. The presence of the ketone in the reaction products was verified by isolation of a semicarbazone with m.p. 173-175° from the initial and intermediate fractions.

By the reaction of 1-butyroxy-1-cyclohexylethane with acetic acid-semicarbazide [1] the semicarbazone of methyl cyclohexyl ketone (49.2%) was obtained with m.p. 173-175° (from alcohol) (mixed m.p. test).

SUMMARY

1. For the first time 3 monosubstituted vinyl β-esters have been synthesized and described: 1-acetoxy-1-cyclohexylethane, 1-propionoxy-1-cyclohexylethane, and 1-butyroxy-1-cyclohexylethane.

2. Hydrolysis of the esters in the presence of acetic acid-semicarbazide was employed as a method of locating the position of the acyloxy groups in the ester molecules.

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INVESTIGATION OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

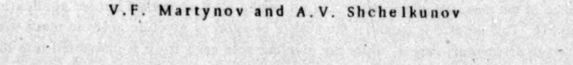
XVII. CONDENSATION OF CHLOROACETONITRILE WITH KETONES. SYNTHESIS OF β,β'-DISUBSTITUTED NITRILES OF GLYCIDIC ACIDS

V.F. Martynov and A.V. Shchelkunov

The nitriles of glycidic acids have been studied very little and there have been only a few investigations devoted to methods of synthesizing them and to the clarification of some of the questions of geometric isomerism encountered in this group of compounds.

The methods described in the literature for the synthesis of nitriles of glycidic acids can be divided into two groups. In one case they were prepared from the nitriles of the corresponding unsaturated acids by preliminary addition of hypochlorous acid to the double bond and subsequent treatment of the chloroxy nitrile formed with alkali [1, 2]. The second method proceeded from the α-chloroketones, which were reacted with alkali cyanides [3-5]. In the latter instance also chloroxy nitriles were intermediate products. It must be noted that both of the methods mentioned have a number of disadvantages. First, in both cases the starting materials are rather difficultly available, to say nothing, of course, of the inconvenience of working with hypochlorous acid and alkali cyanides; second, in the case of the reaction of the α-chloroketones with the alkali cyanides it is largely impossible to synthesize the β,β'-disubstituted nitriles of glycidic acids.

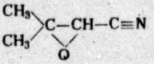
For the synthesis of the β,β'-disubstituted nitriles of glycidic acids we have utilized the Darzens reaction [6]. The only change that we made in this case was to substitute the nitrile of chloroacetic acid for the esters of the α-halogen acids. The reaction in this instance should proceed according to the following equations:



The condensation of chloroacetonitrile with the ketones was carried out under the conditions of Darzens' reaction. A mixture of the nitrile and the appropriate ketone was dissolved in absolute ether and to this ether solution, cooled to −10°, was added dry sodium ethylate. Some excess of the ketone was taken, but a little less than the theoretical amount of sodium ethylate was used.

We carried out the condensation of chloroacetonitrile with five different ketones: acetone, methyl ethyl ketone, cyclopentanone, cyclohexanone, and methyl phenyl ketone.

It must be noted that the condensation of chloroacetonitrile with ketones proceeds more energetically, with a greater evolution of heat than takes place in the case of ethyl chloroacetate. This may be explained by the great lability of the hydrogen atom in the nitrile, inasmuch as the nitrile has a stronger I-effect than the ester grouping. This same fact probably may explain why the nitriles of the glycidic acids are obtained in higher yields than the ethers of the same acids. We prepared five representatives of the β,β'-disubstituted nitriles of glycidic acids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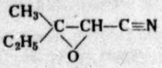
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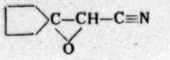
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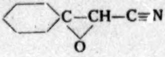
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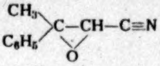
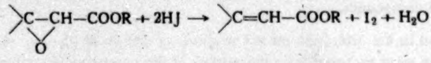

(V)

All the nitriles prepared by us were colorless liquids with a weak but pleasant odor. Upon standing they very quickly darkened with the formation of a brown precipitate. After multiple or double distillation they became more stable.

For evidence of the presence of the oxide ring we used a method worked out for application to the esters of glycidic acids [7]. This method is based on the ability of esters of glycidic acids to react with hydriodic acid with the formation of elementary iodine, while the glycidic acid ester itself is converted into the ester of the corresponding unsaturated acid [8]. The reaction goes according to the equation



As the above-cited authors have shown, the reaction goes quantitatively and is applicable as an analytical method for the determination of oxygen in the three-membered ring of glycidic acids. The accuracy of the determination under our conditions was 0.4-0.6%.

EXPERIMENTAL

Synthesis of the nitrile of β,β'-dimethylglycidic acid. Into a three-necked, 250-ml flask with a mercury seal and a stirrer was poured a mixture of 12 g of chloroacetonitrile and 10.1 g of freshly distilled acetone. Then approximately 100 ml of absolute ether was added, after which the flask with the reaction mixture was cooled with a mixture of ice and salt. When the temperature of the reaction mixture reached −10°, 9.7 g of dry sodium ethylate was added to it in small portions. The reaction proceeded with intense evolution of heat. The process was carried out in such a way that the temperature of the reaction mixture did not exceed 0°. After all the sodium ethylate was added, the contents of the flask were stirred for 30 minutes at −10° and for 1 hour at room temperature. As a result of the reaction that occurred a precipitate of sodium chloride separated. After the stirring was terminated, the reaction mixture was washed with water, the ethereal layer was separated and dried with calcined $MgSO_4$. After distilling off the ether, the residue was distilled in vacuo from a small flask with a herringbone dephlegmator. The nitrile of β,β'-dimethylglycidic acid was a mobile liquid with a slight odor. 9.4 g (67%) was obtained.

B.p. 40-40.5° (10 mm), d_4^{20} 0.9550, n_D^{20} 1.4150, MR_D 25.44; calculated 25.26.

Found %: N 14.39; O 16.93. C_5H_7ON. Calculated %: N 14.43; O 16.70.

Synthesis of the nitrile of β-methyl-β-ethylglycidic acid was carried out as described above. For the reaction 11.8 g of chloroacetonitrile and 15.1 g of freshly distilled methyl ethyl ketone were used. After 100 ml of absolute ether had been added and the mixture cooled to −10°, 7.0 g of dry sodium ethylate was added in small portions. After treatment of the reaction mixture with water, the ethereal extract was dried with $MgSO_4$. The residue after distilling off the ether was distilled in vacuo. The nitrile of β-methyl-β-ethylglycidic acid was a mobile, colorless liquid with a slight odor. 10.8 g (72%) was obtained.

B.p. 46.0-46.5° (10 mm), d_4^{20} 0.9420, n_D^{20} 1.4215, MR_D 29.90; calculated 29.88.

Found %: N 12.60; O 14.76. C_6H_9ON. Calculated %: N 12.61; O 14.41.

Synthesis of the nitrile of β-tetramethyleneglycidic acid was carried out as described above. For the reaction 8.0 g of chloroacetonitrile and 9.8 g of freshly distilled cyclopentanone were used. After 100 ml of absolute ether had been added and the reaction mixture had been cooled to −10°, 6.5 g of dry sodium ethylate was added in small portions. After treatment of the reaction mixture with water, the ethereal extract was dried with $MgSO_4$. The residue after distilling off the ether was distilled in vacuo. The nitrile of β-tetramethyleneglycidic acid was a colorless liquid with a slight odor. 8.5 g (73%) was obtained.

B.p. 93.94° (10 mm), d_4^{20} 1.0200, n_D^{20} 1.4575, MR_D 32.88; calculated 32.30.

Found %: N 11.30; O 13.60. C_7H_9ON. Calculated %: N 11.38; O 13.00.

Synthesis of the nitrile of β-pentamethyleneglycidic acid was carried out as described above. For the reaction 10.5 g of chloroacetonitrile and 14.8 g of freshly distilled cyclohexanone were used. To the mixture of these materials was added 100 ml of absolute ether. After the necessary cooling, 8.6 g of dry sodium ethylate was added in small portions. After treatment of the reaction mixture with water, the ethereal extract was dried with $MgSO_4$. The residue after distilling off the ether was distilled in vacuo. The nitrile of β-pentamethyleneglycidic acid was a clear, colorless liquid with a slight odor. 11.2 g (65%) was obtained.

B.p. 84-84.5° (5 mm), d_4^{20} 1.0275, n_D^{20} 1.4665, MR_D 36.98; calculated 36.92.

Found %: N 9.99; O 11.21. $C_8H_{11}ON$. Calculated %: N 10.22; O 11.75.

Synthesis of the nitrile of β-methyl-β-phenylglycidic acid was carried out as described above. For the reaction 13.8 g of chloroacetonitrile and 23.3 g of freshly distilled acetophenone were used. To the mixture of these materials was added 100 ml of absolute ether. After the necessary cooling 11.0 g of dry sodium ethylate was added in small portions. After treatment of the reaction mixture with water, the ethereal extract was dried with $MgSO_4$. The residue after distilling off the ether was distilled in vacuo. The nitrile of β-methyl-β-phenylglycidic acid was a colorless, clear liquid with a slight odor. 20.0 g (80%) was obtained.

B.p. 128-128.5° (7 mm), d_4^{20} 1.0520, n_D^{20} 1.5147, MR_D 44.48; calculated 44.75.

Found %: N 8.91; O 10.51. $C_{10}H_9ON$. Calculated %: N 8.80; O 10.06.

SUMMARY

1. The reaction of chloroacetonitrile under the conditions of the Darzens reaction with aliphatic, polymethylenic, and aliphatic-aromatic ketones has been investigated.

2. Five nitriles of glycidic acids that had not been described in the literature have been synthesized.

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INVESTIGATION OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

XVIII. REACTION OF THE ETHYL ESTER OF β-TETRAMETHYLENEGLYCIDIC ACID WITH AROMATIC AMINES

V.F. Martynov

In one of our previous communications [1] we have described the addition of aniline to the ethyl ester of β-tetramethyleneglycidic acid and the subsequent conversion of the addition product to tetrahydrocarbazole. The present investigation is a continuation of this study. In it we set up as our goal the investigation of the possibility of synthesizing various homologs and substitution products of 1,2,3,4-tetrahydrocarbazole.

Since the method developed by us for the synthesis of the tetrahydrocarbazole included the preliminary preparation of α-hydroxy-β-arylamino-β-tetramethylenepropionic acid, we first studied the reaction of addition of various aromatic amines to the ethyl ester of β-tetramethyleneglycidic acid. This specific glycidic acid is most reactive; therefore the stearic factors that usually hinder the addition reaction must here play a secondary rôle, as a result of which the course of the reaction must be dependent on the reactivity of the amine group.

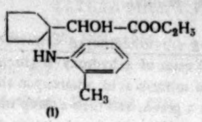
As aromatic amines we chose o-, m-, and p-toluidine, β-naphthylamine, and o-, m-, and p-nitroaniline. With the toluidines and β-naphthylamine we obtained the corresponding addition products, which are shown in the chart; as for o-, m-, and p-nitroaniline, addition products were not obtained with them. Upon heating the ester of the glycidic acid with o- or p-nitroaniline in a sealed ampoule, explosions occurred regardless of whether we carried out the reaction with or without a solvent (ethyl alcohol). When the reaction was carried out with m-nitroaniline, an explosion did not occur, but still no addition product was formed.

We subjected the addition products, which were prepared for the purpose of converting them to the tetrahydrocarbazoles, to the action of concentrated sulfuric acid. In the case of the ethyl esters of α-hydroxy-β-(o- or p-toluidino)-β-tetramethylenepropionic acid (I and V) we obtained well-defined products, corresponding to the methyltetrahydrocarbazoles (II and VI). Upon decomposition of the ethyl ester of α-hydroxy-β-(m-toluidino)-β-tetramethylenepropionic acid (III) we might expect, according to the earlier adduced reaction mechanism [1], two products: 5-methyl-1,2,3,4-tetrahydrocarbazole (IVa) and 7-methyl-1,2,3,4-tetrahydrocarbazole (IVb). The product obtained by us in fact appeared nonhomogeneous; first, it did not have, like the rest of the indoles, a clearly defined leaflike crystal form, but was a finely crystalline precipitate; second, and especially important, it did not have, like the other carbazoles, a sharp melting point, but an extended one.

An analogous case has been pointed out in the literature. Upon ring closure by the method of Borsh, the 3-nitrophenylhydrazone of cyclohexanone yields a mixture of 5- and 7-nitrotetracarbazoles [2, 3].

By decomposition with sulfuric acid of the ethyl ester of α-hydroxy-β-(β-naphthylamino)-β-tetramethylenepropionic acid (VII) we obtained not a crystalline product, as might have been expected, but a viscous greenish-brown mass. This could be explained by the fact that on treatment with sulfuric acid under conditions of heating to 120° there occurs a preliminary sulfonation of the β-naphthylamine group and consequently there is obtained not the carbazole itself, but its sulfo derivative (VIII), which is a viscous substance.

Actually, as shown by analysis, we did have the sulfo derivative which we obtained in a crystalline condition as the sodium salt. A similar compound, only without the sulfo group, was obtained by Borsche [5]. We did not establish the position of the sulfo group.



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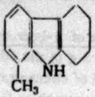

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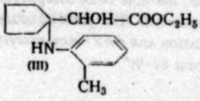

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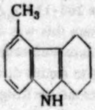
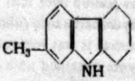


(IVa)



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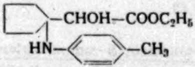

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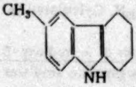
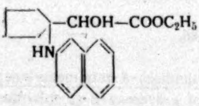
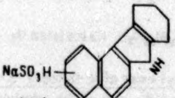


(VI)



(VII)



(VIII)

EXPERIMENTAL

Synthesis of the ethyl ester of α-hydroxy-β-(o-toluidino)-β-tetramethylenepropionic acid (I). 10 g of the ethyl ester of β-tetramethyleneglycidic acid was heated in a sealed ampoule with 18 g of o-toluidine for 20 hours at 160-170°. The dark red reaction mass was distilled in vacuo and a light green, viscous liquid was obtained. The substance was purified by repeated distillation. 7.4 g (46%) was obtained.

B.p. 135-136° (0.5 mm), d_4^{20} 1.1105, n_D^{20} 1.5445, MR_D 78.80; calculated 76.07. EM_D 2.73.

Found %: N 5.27. $C_{16}H_{23}O_3N$. Calculated %: N 5.05.

Conversion of the ethyl ester of α-hydroxy-β-(o-toluidino)-β-tetramethylenepropionic acid to 8-methyl-1,2,3,4-tetrahydrocarbazole (II). To 4 g of the ethyl ester of α-hydroxy-β-(o-toluidino)-β-tetramethylenepropionic acid was added 15 ml of concentrated sulfuric acid, after which the reaction mixture was heated over a bare flame with continuous stirring with a thermometer. During heating the materials dissolved in each other and the solution became very dark. When the temperature of the reaction mixture reached 100°, bubbles of carbon monoxide began to be evolved from the solution. At 110-115° decomposition proceeded very vigorously. When the evolution of carbon monoxide ceased, the hot solution was poured over ice; thereupon a dark gray substance separated, which was filtered off and subjected to steam distillation. After this the material was twice recrystallized from aqueous alcohol, and in this way 0.7 g (30%) of lamellar crystals with an oily lustre were obtained. M.p. 96-97°.

Picrate – dark brown needles, m.p. 118-119°. Literature data: m.p. 98° [4].

Synthesis of the ethyl ester of α-hydroxy-β-(m-toluidino)-β-tetramethylenepropionic acid (III). 5 g of the ethyl ester of β-tetramethyleneglycidic acid was heated in a sealed ampoule with 9 g of m-toluidine for 8 hours at 160-180°. The contents of the ampoule darkened slightly. The reaction mass was subjected to distillation in vacuo; in this way a greenish, viscous liquid was separated which quickly crystallized. When the experiment was repeated, the substance started to crystallize upon cooling in the reaction ampoule itself, and in this instance the vacuum distillation was not carried out. After recrystallization from ligroin 6 g (75%) of colorless, needle-shaped crystals was obtained. B.p. 143-145° (0.5 mm), m.p. 83-84°.

Found %: N 4.84. $C_{16}H_{23}O_3N$. Calculated %: N 5.05.

Conversion of the ethyl ester of α-hydroxy-β-(m-toluidino)-β-tetramethylenepropionic acid to methyl-1,2,3,4-tetrahydrocarbazole (IV). 3 g of the ethyl ester of α-hydroxy-β-(m-toluidino)-β-tetramethylenepropionic acid was dissolved in 10 ml of concentrated sulfuric acid, whereupon slight darkening of the solution was observed. Upon heating, the solution took on first a green, and then a deep indigo color. Decomposition with the evolution of carbon monoxide occurred at 100-110°. After the evolution of carbon monoxide bubbles ceased, the reaction mixture was poured over ice; when this was done, the blue color disappeared and an abundant precipitate of methyltetrahydrocarbazole (chocolate-colored) separated. The yield of crude product was quantitative. To purify the material it was subjected to steam distillation and then twice recrystallized from aqueous alcohol. Fine crystals were obtained with a broad melting point 82-90°.

Found %: N 7.62. $C_{13}H_{15}N$. Calculated %: N 7.57.

Synthesis of the ethyl ester of α-hydroxy-β-(p-toluidino)-β-tetramethylenepropionic acid (V). 5 g of the ethyl ester of β-tetramethyleneglycidic acid was heated in a sealed ampoule with 6 g of p-toluidine for 6 hours at 160-180°. The reaction product started to crystallize in the ampoule; it was pressed out and recrystallized several times from ligroin; 4 g (50%) of needle-shaped crystals were obtained. M.p. 94-95°.

Found %: N 5.23. $C_{16}H_{23}O_3N$. Calculated %: N 5.05.

Conversion of the ethyl ester of α-hydroxy-β-(p-toluidino)-β-tetramethylenepropionic acid to 6-methyl-1,2,3,4-tetrahydrocarbazole (VI). 3 g of the ethyl ester of α-hydroxy-β-(p-toluidino)β-tetramethylenepropionic acid was dissolved in 10 ml of concentrated sulfuric acid and the reaction mixture was heated over a bare flame. At 100-110° vigorous evolution of carbon monoxide was observed. After pouring over ice, an abundant, crystalline, gray-colored precipitate separated. The yield of crude product was quantitative. To purify the material it was steam-distilled and recrystallized twice from aqueous alcohol. Colorless crystals with a pearly luster were obtained. M.p. 135-136°. Literature data: m.p. 141-142° [5].

Synthesis of the ethyl ester of α-hydroxy-β-(β-naphthylamino)-β-tetramethylenepropionic acid (VII). 5 g of the ethyl ester of β-tetramethyleneglycidic acid and 4.2 g of β-naphthylamine (equimolecular quantities) were dissolved in 20 ml of anhydrous alcohol, sealed in an ampoule, and heated for 6 hours at 160-170°. The next day crystals of the addition product had precipitated in the ampoule. They were pressed out and recrystallized from petroleum ether. 5 g (54%) of needle-shaped crystals were obtained. M.p. 114-115°.

Found %: N 4.51. $C_{19}H_{24}O_3N$. Calculated %: N 4.47.

Conversion of the ethyl ester of α-hydroxy-β-(β-naphthylamino)-β-tetramethylenepropionic acid to the sulfo derivative of 1,2,3,4-tetrahydro-5,6-benzocarbazole (VIII). 1 g of the ethyl ester of α-hydroxy-β-(β-naphthylamino)-β-tetramethylenepropionic acid was heated with 5 ml of concentrated sulfuric acid. The solution acquired a dark red color. Vigorous decomposition with the evolution of carbon monoxide was observed at 115-120°. After the evolution of gas bubbles had ceased, the reaction mass was poured over ice, whereupon a viscous, greenish-brown substance separated. It was recovered with the aid of a spatula and dissolved in a small amount of alcohol. To the alcohol solution was added the calculated amount of aqueous NaOH solution, and a white crystalline precipitate immediately formed. After recrystallization from aqueous alcohol the material was obtained as lamellar crystals with an oily luster.

Found %: N 4.4; S 10.2. $C_{16}H_{15}O_3NSNa$. Calculated %: N 4.6; S 9.9.

SUMMARY

1. The reaction of the ethyl ester of β-tetramethyleneglycidic acid with aromatic amines has been investigated. Four ethyl esters of α-hydroxy-(β-arylamino)-β-tetramethylenepropionic acid that had not been described in the literature have been prepared.

2. The conversion of the esters of α-hydroxy-(β-arylamino)-β-tetramethylenepropionic acids that were obtained to the corresponding tetrahydrocarbazoles has been accomplished.

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*Original Russian pagination. See C.B. translation.

OXIDATIVE BREAKDOWN OF THE OZONIDE OF BUTADIENE RUBBER

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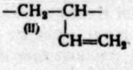
It has been established [1, 2] that the molecule of butadiene rubber contains 1,4- (I) and 1,2- (II) chains.

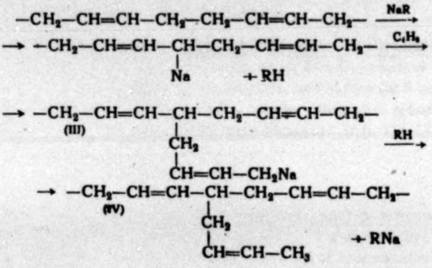
$-CH_2-CH=CH-CH_2-$ (I)



(II)

$-CH_2-\underset{\underset{CH=CH_2}{|}}{CH}-$

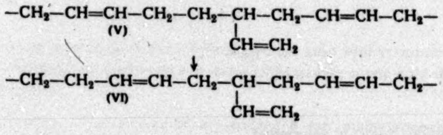
The relative positions of the 1,4- and 1,2-chains in the rubber molecule can be determined on the basis of study of the products of ozonolysis of butadiene rubbers. Marvel [3] carried out the oxidative breakdown of the ozonides of butadiene rubbers and fractionated the products of ozonolysis by the method of partition chromatography. Formic acid, succinic acid, 1,2,4-butanetricarboxylic acid and 1,x,y,6-hexanetetracarboxylic acid have been found among the products of ozonolysis of butadiene rubbers [4, 6]. These could be formed, respectively, from portions of the rubber molecule involving the following chains: 1,2; 1,4-1,4; 1,4-1,2-1,4; and 1;4-(1,2)$_x$-1,4. Marvel found 1,2,3-propanetricarboxylic acid in addition to the above acids. 1,2,3-Propanetricarboxylic acid might be derived from branched portions of the rubber molecule formed, for example, by metalation at the α-methylene group.



$-CH_2-CH=CH-CH_2-CH_2-CH=CH-CH_2-$
NaR
$\rightarrow -CH_2-CH=CH-CH-CH_2-CH=CH-CH_2-$
C_6H_6
Na
+ RH
$\rightarrow -CH_2-CH=CH-CH-CH_2-CH=CH-CH_2-$
(III)
CH_2
RH
$CH=CH-CH_2Na$
$\rightarrow -CH_2-CH=CH-CH-CH_2-CH=CH-CH_2-$
(IV)
CH_2
+ RNa
$CH=CH-CH_3$

In portion (III) the side chain may grow or the sodium may be replaced by hydrogen, and chain growth will be stopped. Independently of the length of the side chain, 1,2,3-propanetricarboxylic acid will be formed from portion (IV) of the rubber molecule when the ozonide undergoes oxidative breakdown.

The possibility of formation of 1,2,3-propanetricarboxylic acid from portion (VI) of the macromolecule is not excluded; the latter type of chain could be formed by rearrangement of the double bonds in presence of an alkali metal [7].



$-CH_2-CH=CH-CH_2-CH_2-CH-CH_2-CH=CH-CH_2-$
(V)
$CH=CH_2$
$-CH_2-CH_2-CH=CH-CH_2-CH-CH_2-CH=CH-CH_2-$
(VI)
$CH=CH_2$

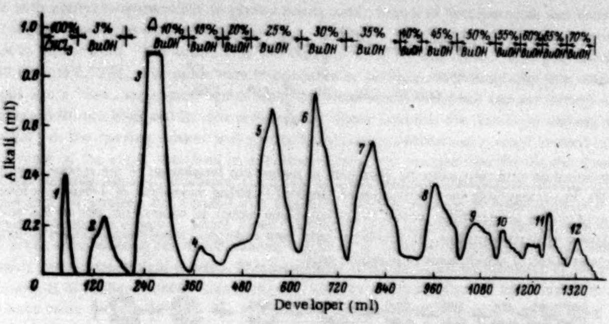


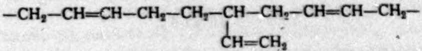
Fig. 1. Chromatogram of viscous acids obtained by oxidative decomposition of rubber ozonide with acetyl hydroperoxide: 1) not identified; 2) levulinic acid; 3) acetic acid; 4) formic acid; 5) succinic acid; 6) 1,2,4-butanetricarboxylic acid; 7) 1,2,3-propanetricarboxylic acid; 8) 1,x,y,6-hexanetetracarboxylic acid; 9-12) not identified.

On the other hand the presence of 1,2,3-propanetricarboxylic acid in the products of ozonolysis of butadiene rubber might be accounted for by secondary reactions under certain conditions of ozonolysis. Marvel [3], for example, failed to find this acid among the products of ozonolysis of the ozonide of butadiene rubber under mild conditions.

Clarification of the routes of formation of 1,2,3-propanetricarboxylic acid is very important since its presence in the products of ozonolysis might be an indication of a branched structure of the macromolecule of rubber.

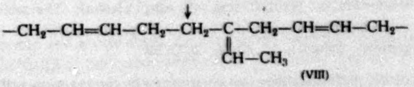
We carried out oxidative decomposition of the ozonide of butadiene rubber prepared at 5° under various conditions. Decomposition of the ozonide with acetyl hydroperoxide and decomposition with 3% hydrogen peroxide at 60°* led to the appearance of 1,2,3-propanetricarboxylic acid among the products of ozonolysis (Figure 1, peak 7; Figure 2, peak 6). We therefore put forward the hypothesis that 1,2,3-propanetricarboxylic acid originated from portions of the macromolecule of the polymer linked by 1,4-1,4-chains with branching at the α-methylene group, or from 1,4-1,2-1,4-chains in which the double bonds underwent rearrangement. This rearrangement could have taken place during polymerization [7] or ozonization [8].

We detected levulinic acid (Figure 1, peak 2) among the products of ozonolysis after oxidative decomposition of the ozonide of butadiene rubber with acetyl hydroperoxide. Marvel [3] found levulinic acid in the products of ozonolysis of emulsion rubber. This acid may result from the formation of chains with structure (VIII) due to rearrangement of the double bonds in (VII) [7, 8].



$$-CH_2-CH=CH-CH_2-CH_2-\underset{\displaystyle CH=CH_2}{\underset{|}{CH}}-CH_2-CH=CH-CH_2-$$

(VII)



$$-CH_2-CH=CH-CH_2-\overset{\downarrow}{CH_2}-\underset{\displaystyle CH-CH_3}{\underset{\|}{C}}-CH_2-CH=CH-CH_2-$$

(VIII)

Ozonization followed by oxidative decomposition of the ozonide leads to formation of β-ketoadipic acid from the portion (VIII) of the macromolecule. Partial decarboxylation of the latter acid can yield levulinic acid.

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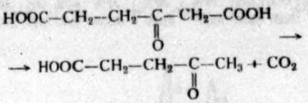
*Marvel did not find 1,2,3-propanetricarboxylic acid when the ozonide was heated with 3% hydrogen peroxide for 3 hours at 60° and for 30 minutes at 100°.



$$\mathrm{HOOC{-}CH_2{-}CH_2{-}\underset{\underset{O}{\|}}{C}{-}CH_2{-}COOH} \rightarrow$$

$$\rightarrow \mathrm{HOOC{-}CH_2{-}CH_2{-}\underset{\underset{O}{\|}}{C}{-}CH_3 + CO_2}$$

Formation of levulinic acid might also be attributed to anomalous breakdown of the rubber ozonide containing chains of (II), in analogy with the observation of Ziegler [9] during ozonolysis of 4-vinylcyclohexane-1. β-Hydroxyadipic acid can be formed from portion (V) of butadiene rubber on ozonolysis, due to the performate rearrangement followed by decomposition. The hydroxy-acid then undergoes transformation into β-ketoadipic acid, partial decarboxylation of which leads to levulinic acid.

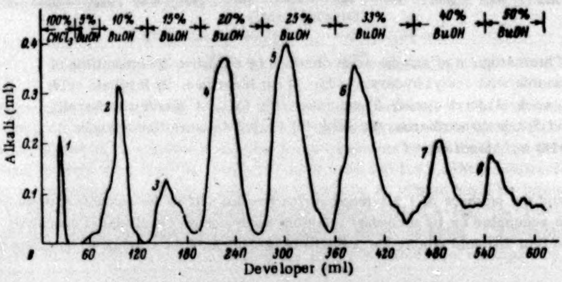


Fig. 2. Chromatogram of viscous acids obtained by oxidative decomposition of rubber ozonide with hydrogen peroxide: 1) not identified; 2) acetic acid; 3) formic acid; 4) succinic acid; 5) 1,2,4-butanetricarboxylic acid; 6) 1,2,3-propanetricarboxylic acid; 7) 1,x,y,6-hexanetetracarboxylic acid; 8) not identified.

Levulinic acid was not found in the products of oxidative decomposition of the ozonide of butadiene rubber with 3% hydrogen peroxide. In an oxidizing medium this acid could undergo further oxidation with formation of succinic acid, acetic acid and other oxidation products.

Due to the fact that oxidative decomposition of rubber ozonide with acetyl hydroperoxide was conducted in an acetic acid medium, we could not assume that acetic acid (Figure 1, peak 3) was a product of ozonolysis of rubber. Acetic acid was present, however, in the products of oxidative breakdown of the ozonide with 3% hydrogen peroxide (Figure 2, peak 2). In this case its formation may be attributed to the ozonolysis of chains (IV) and (VIII) and to breakdown in the oxidizing medium of the levulinic acid formed.

EXPERIMENTAL

Butadiene rubber, prepared by polymerization of butadiene in presence of 0.5% metallic sodium at 5°, was purified by dissolving twice in benzene and precipitating with ethyl alcohol. The rubber was dried to constant weight at room temperature and a residual pressure of 2 mm. All operations with the rubber were conducted in an oxygen-free nitrogen atmosphere. Found %: C 87.74; H 11.29.

The total unsaturation of the purified rubber was determined by the reaction with iodine bromide [10]; it was 88%. The percentage of 1,2-chains was found from the quantity of formaldehyde and formic acid among the products of decomposition of the ozonide of the rubber with water [11]. Chains with terminal double bonds constituted 65.5%.

The rubber ozonide was next oxidatively decomposed with acetyl hydroperoxide. Rubber (4.95 g) was ozonized in ethyl acetate (b.p. 77-78°) at −20°. The solvent was distilled off at 20° and 10 mm. The ozonide was decomposed with acetyl hydroperoxide in glacial acetic acid. Excess of hydroperoxide was destroyed with platinum black (negative reaction with potassium iodide). Aldehydes were not detected in the solution of products of ozonolysis in acetic acid. The acetic acid was distilled off at 40° and 2 mm. 9.39 g of viscous acids was obtained (C 40.88%, H 6.12%). The acids were fractionated by partition chromatography in a column of silica gel. The silica gel was a "fine, large-pore" grade from the Voskresensky works and was put through a 150-mesh sieve. The column was 160 mm high and 25 mm in diameter. Water served as the stationary solvent, and chloroform (b.p. 60.5-61.5°) as the moving solvent with gradually increasing additions of n-butyl alcohol (b.p. 117-118°). A weighed sample of the acids, dissolved in tert-amyl alcohol was charged into the column through which was then passed the washing liquid ("developer") at a rate of 1 ml/minute. The solution flowing through the column was collected in 3 ml portions and titrated with alcoholic alkali in presence of phenolphthalein. The chromatographic curve is plotted in Figure 1, which shows the elution peaks characterizing the acids in the mixture. The recovery of acids after washing out of the column was 98-99%. Data were calculated on the basis of several chromatograms giving concordant results. Chromatograms obtained in the fractionation of the acids of the products of ozonolysis of rubber ozonide were compared with the chromatograms of mixtures of the acids that were claimed to have been detected (Figure 3). In the latter diagram there is no peak corresponding to hexanetetracarboxylic acid. It is known from previous data, however, that after propanetricarboxylic acid has been treated with a solution containing 55% chloroform and 45% n-butyl alcohol, hexanetetracarboxylic acid is eluted.

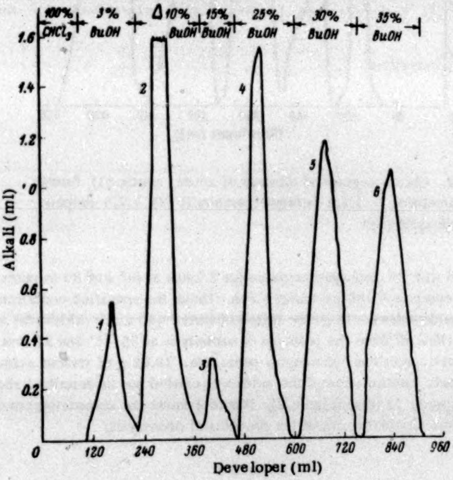


Fig. 3. Chromatogram of mixture of acids: levulinic (1), acetic (2), formic (3), succinic (4), 1,2,4-butanetricarboxylic (5), 1,2,3-propanetricarboxylic (6).

After deducting the formic and acetic acids, the products of oxidative breakdown of rubber ozonide with acetyl hydroperoxide contain 71.2% of the carbon skeleton, as calculated from the chromatograms. The formic acid originating from the 1,2-chains in the rubber molecule also came off when the acetic acid was distilled off from the products of ozonolysis. The investigated rubber contains 65.5% of 1,2-chains, which on ozonolysis must lead to formaldehyde and formic acid containing 16.4% of the carbon skeleton. The carbon skeleton is thus accounted for to the extent of 87.6% in the products of ozonolysis.

Oxidative decomposition of rubber ozonide with hydrogen peroxide was carried out after 7.57 g of rubber had been ozonized and the solvent distilled off under the same conditions (see above). After removal of the sol-

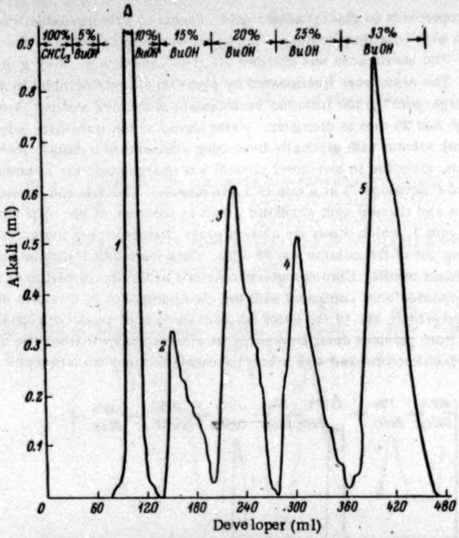


Fig. 4. Chromatogram of mixture of acids: acetic (1), formic (2), succinic (3), 1,2,4-butanetricarboxylic (4), 1,2,3-propanetricarboxylic (5).

vent, the ozonide was heated with 3% hydrogen peroxide for 3 hours at 60° and 30 minutes at 100°. The excess of hydrogen peroxide was decomposed with platinum black. Under the specified conditions of oxidative decomposition of the ozonide, the aldehydes could not be fully converted into acids (aldehydes were detected by qualitative tests). Water was distilled off from the products of ozonolysis at 35-40° and 25 mm, and the last traces were removed in a vacuum desiccator over phosphorus pentoxide. 10.68 g of viscous acids (C 42.76%, H 6.06%) was obtained. Chromatographic fractionation of the acids was carried out as described above but in a smaller column (height 160 mm, diameter 15 mm) (Figure 2). Figure 4 shows the chromatogram of the suggested mixture of acids in comparison with the chromatogram of the products of ozonolysis.

SUMMARY

1. Among the products of oxidative decomposition with acetyl hydroperoxide of the ozonide of butadiene rubber (prepared at 5°) are levulinic, formic, succinic, 1,2,4-butanetricarboxylic, 1,2,3-propanetricarboxylic and 1,x,y,6-hexanetetracarboxylic acids. Levulinic acid could be formed by isomerization of 1,4-1,2-1,4-chains of the rubber macromolecule and by partial decarboxylation of β-ketoadipic acid, as well as by the peroxy-formate rearrangement in presence of acetyl hydroperoxide. 1,2,3-Propanetricarboxylic acid is more likely to be formed from 1,4-1,4-chains branched at the α-methylene group, or from 1,4-1,2-1,4-chains in which the double bonds had undergone suitable rearrangement, rather than as a result of secondary reactions during oxidative breakdown of the ozonide. 1,2,3-Propanetricarboxylic acid was also detected among the products of ozonolysis obtained under mild conditions of breakdown.

2. Products of oxidative breakdown of the ozonide of the rubber in question with hydrogen peroxide were acetic, formic, succinic, 1,2,4-butanetricarboxylic, 1,2,3-propanetricarboxylic and 1,x,y,6-hexanetetracarboxylic acids. Acetic acid could have been formed from 1,4-1,4-portions of the rubber molecule branched at the α-methylene group, as well as from isomerized 1,4-1,2-1,4-portions.

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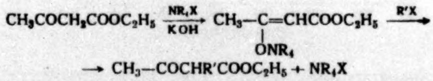
ALKYLATION IN AN AQUEOUS MEDIUM IN PRESENCE OF QUATERNARY AMMONIUM SALTS. III.

A.T. Babayan and M.G. Indzhikyan

It was previously shown that catalytic amounts of quaternary ammonium salts in an aqueous alkaline medium can bring about the alkylation of ethyl acetoacetate, acetylacetone, diethyl malonate [1], and aromatic amines [2]. This reaction is entirely different in character from the alkylation with the help of quaternary ammonium salts at high temperatures [1].

The hypothesis was advanced that alkylation in our experiments proceeds via the stage of formation of tetraalkyl-ammonium derivatives of the compounds undergoing alkylation.



$$CH_3COCH_2COOC_2H_5 \xrightarrow[KOH]{NR_4X} CH_3{-}\underset{\displaystyle ONR_4}{\underset{|}{C}}{=}CHCOOC_2H_5 \xrightarrow{R'X}$$

$$\rightarrow CH_3{-}COCHR'COOC_2H_5 + NR_4X$$

The present paper is devoted to the verification of this hypothesis and to further study of the reaction.

Experiments on the alkylation of ethyl acetoacetate with 1,3-dichlorobutene-2 in presence of 1 N solutions of tetramethylammonium hydroxide (I), trimethylphenylammonium hydroxide (II) and dimethyldibenzylammonium hydroxide (III) showed that potassium hydroxide can be replaced by quaternary ammonium bases. Results of these experiments, as well as of experiments on alkylation with the help of potassium hydroxide of the same concentration in the presence and absence of catalytic quantities of dimethyldibenzylammonium chloride, are presented in Table 1.

In the alkylation of ethyl acetoacetate, acetylacetone, phenol and benzyl alcohol (Table 2) the yields obtained with dimethyldibenzylammonium hydroxide exceeds the yields obtained under the action of potassium hydroxide, and they are similar to those obtained under the action of 10 N potassium hydroxide in presence of catalytic amounts of dimethyldibenzylammonium chloride.

TABLE 1

Alkylation of Ethyl Acetoacetate with 1,3-Dichlorobutene-2 under the Action of 1 N Solutions of Quaternary Ammonium Bases (I), (II) and (III), and also under the Action of 1 N Solutions of Potassium Hydroxide in Presence and Absence of a Catalytic Amount of the Chloride of Base (III)

Base taken		Hydroxide of			KOH	KOH and dimethyldibenzylammonium chloride
		tetramethylammonium (I)	trimethylphenylammonium (II)	dimethyldibenzylammonium (III)		
Yield (in %)	mono	23.7	36.5	53.0	19	30.9
	total	23.7	40.8	68.5	19	30.9

In the alkylation of o-toluidine and ethylaniline the yields in presence of dimethyldibenzylammonium hydroxide are the same as under the action of potassium hydroxide and lower than those under the action of potassium hydroxide plus catalytic quantities of dimethyldibenzylammonium chloride. The cause of this difference has not yet been established.

TABLE 2

Alkylation of Ethyl Acetoacetate, Acetylacetone, Phenol, Benzyl Alcohol, Ethylaniline and o-Toluidine with 1,3-Dichlorobutene-2 under the Action of 1 N Solution of (IV), and Likewise under the Action of 1 and 0.1 N Solutions of Potassium Hydroxide in Presence and Absence of a Catalytic Quantity of the Chloride of Base (III)

Compound alkylated	Yield (in %)									
	1 N KOH		1 N dibenzylammonium hydroxide		1 N KOH and dimethyldibenzylammonium chloride		10 N KOH		10 N KOH and dimethyldibenzylammonium hydroxide	
	mono	total	mono	total	mono	total	mono	total	mono	total
Ethyl acetoacetate	19	19	53	68.5	30.9	30.9	42	42	56.6	74.3
Acetylacetone	50	50	63	70	55.8	55.8	45	45	53.6	64.8
Phenol	40	50	56.3	71	47.1	71.4	30.6	77.6	46.5	67.5
Benzyl alcohol	5.8	5.8	52.4	52.4	42.5	42.5	40.0	40.0	63.8	63.8
Ethylaniline	31.9	31.9	36	36	–	–	–	–	52.8	52.8
o-Toluidine	31.1	31.1	31.9	31.9	41.9	41.9	42.3	42.3	59.5	59.5

It should be noted that all of the experiments whose results are presented in the above and subsequent tables are readily reproducible, the variations in yields amounting to not more than 1%. The only exceptions are the experiments on alkylation of aromatic amines where yields varying by up to 10% and more are sometimes obtained.

For further verification of the reaction mechanism we prepared the dimethyldibenzylammonium derivative of phenol and studied its behavior in alkylations with 1,3-dichlorobutene-2. We prepared this phenate by the method employed by Tarbell and Vaughan [3] for preparation of dimethallylphenylammonium 2,6-dimethylphenate, but with a slight modification. Unlike the sodium phenate, the dimethyldibenzylammonium phenate is insoluble in ether. There is here an analogy with the solubility of tetraalkylammonium and metallic enolates of diphenylpropiomesitylene [4] in ether.

Interaction of dimethyldibenzylammonium phenate with 1,3-dichlorobutene-2 in ethereal solution gave 3-chlorobutene-2-phenyl ether in 43.7% yield. The yield of the same ether when sodium phenate was alkylated under the same conditions was 12.7%. The result of alkylation of the prepared tetraalkylammonium derivative is therefore another indication of the correctness of the proposed reaction mechanism.

TABLE 3

Alkylation of Ethyl Acetoacetate with 1,3-Dichlorobutene-2 under the Action of 10.5 and 1 N Solutions of Potassium and Sodium Hydroxides, a 5 N Solution of Lithium Hydroxide, and 5 N and 1 N Solutions of Tetramethylammonium Hydroxide

Formula and normality of alkali	KOH			NaOH			LiOH	$(CH_3)_4NOH$	
	10	5	1	10	5	1	5	5	1
Yield (in %)	42	21.6	19	45	24.7	19	36.1	29.7	23.7

Results of investigations set forth in Table 3 show that the concentration and nature of the caustic alkali have a strong influence on the yield of alkylated product. On passing, for example, from 10 N potassium hydroxide solution to 5 N solution, the yield of alkylation product is roughly halved, but further dilution scarcely affects the yield. A comparison of the yields of products of alkylation under the action of lithium, sodium and potassium hydroxides shows that yields rise with falling basicity.

Halides of alkali metals likewise influence the yield. The yield of products of alkylation of ethyl acetoacetate under the action of 10 N solutions of sodium and potassium hydroxides increases on addition of equimolar quantities of halides of the same metals (Table 4).

TABLE 4

Alkylation of Ethyl Acetoacetate with 1,3-Dichlorobutene-2 under the Action of 10 N Solutions of Potassium and Sodium Hydroxides and in the Presence and Absence of Equimolar Quantities of Sodium and Potassium Chlorides

Alkali and added salt	KOH			NaOH		
	–	KCl	NaCl	–	KCl	NaCl
Yield (in %)	42.0	46.5	50.8	45.0	51.7	52.5

According to Table 4 the best yield is obtained when ethyl acetoacetate is alkylated with 1,3-dichlorobutene-2 under the action of sodium hydroxide plus sodium chloride, the yield being then equal approximately to that of the monoalkylated derivative under the action of potassium hydroxide plus a catalytic quantity of dimethyldibenzylammonium chloride.

In another experiment, ethyl acetoacetate was alkylated under the action of 5 N sodium hydroxide solution with addition of half of the equimolar quantity of lithium chloride; 5 N alkali was used instead of 10 N solution in this case in order to avoid precipitation of lithium hydroxide. Experiments with additions of sodium and potassium chlorides were run for comparison. As we see from Table 5, the highest yield is obtained when lithium chloride is added, the yield then equaling the yield under the action of 5 N lithium hydroxide.

TABLE 5

Alkylation of Ethyl Acetoacetate with 1,3-Dichlorobutene-2 under the Action of 5 N Sodium Hydroxide Solution in Presence of Potassium, Sodium and Lithium Chlorides

Alkali and added salt	NaOH				LiOH
	–	KCl	NaCl	LiCl	
Yield (in %)	24.7	28.6	29.6	34.1	36.1

The above data are in harmony with those presented in Table 6. The latter table shows that the yield of products of alkylation of ethyl acetoacetate under the catalytic action of dimethyldibenzylammonium chloride is substantially independent of the nature of the alkali used.

TABLE 6

Alkylation of Ethyl Acetoacetate with 1,3-Dichlorobutene-2 under the Action of 5 N Solutions of Potassium, Sodium, Lithium and Tetramethylammonium Hydroxides in Presence of a Catalytic Quantity of the Chloride of Base (III)

5 N alkali taken		KOH	NaOH	LiOH	$(CH_3)_4NOH$
Yield (in %)	mono	62.6	60.0	59.0	60.0
	total	73.3	74.3	61.3	68.0

EXPERIMENTAL

1. Alkylation of dimethyldibenzylammonium phenate with 1,3-dichlorobutene-2 in an ethereal medium.

To a solution of 1.93 g metallic sodium in 45 ml anhydrous ethyl alcohol were added 7.9 g freshly distilled phenol and a solution of 21.9 g dimethyldibenzylammonium chloride in 30 ml anhydrous ethyl alcohol. The precipitated sodium chloride was filtered off (4.8 g, 98%), the ethyl alcohol was evaporated off in vacuo at room temperature, and 500 ml absolute ether was added to the residue. After a few days, the ether-insoluble viscous mass crystallized; m.p. 110-112°. A molecular weight of 313 was found by decomposing a weighed sample with water and titrating the resultant hydroxide. Calculated for dimethyldibenzylammonium phenate: M 319. 12.5 g 1,3-dichlorobutene-2 was added to a suspension of the phenate in ether; the mixture was stirred for 2 hours at the boiling point of ether. It was then diluted with water; the lower layer and the ethereal extract of the upper layer were washed free of phenol with caustic alkali, and dried; the solvent was driven off, and the residue fractionated in vacuo to give 7.24 g (47.3%) 3-chlorobuten -2-yl-phenyl ether.

B.p. 106-109° (5 mm), d_4^{20} 1.1150, n_D^{20} 1.5344, MR_D 50.90. $C_{10}H_{11}OCl\digamma_4$. Calculated 51.02 [5].

2. Alkylation of sodium phenate. To a solution of 2.3 g metallic sodium in 45 ml anhydrous ethyl alcohol was added 9.4 g freshly distilled phenol. The ethyl alcohol was driven off in vacuo at room temperature, and 500 ml ether was added to the residual white crystals which dissolved completely. After addition of 12.5 g 1,3-dichlorobutene-2, the mixture was stirred for 2 hours at the boiling point of ether. The solution was diluted with water; the lower layer, together with the ether extract of the upper layer, was washed free of phenol with caustic alkali, the solvent was driven off, and the residue was fractionally distilled in vacuo to give 2.32 g (12.7%) 3-chlorobuten-2-yl-phenyl ether with b.p. 110-112° (10 mm).

3. Alkylation of ethylaniline with 1,3-dichlorobutene-2 under the action of dimethyldibenzylammonium hydroxide. A mixture of 12.1 g ethylaniline, 12.5 g 1,3-dichlorobutene-2 and 100 ml of 1 N solution of dimethyldibenzylammonium hydroxide was stirred for 25 minutes on a boiling water bath. The top layer was separated and acidified; the unreacted 1,3-dichlorobutene-2 was removed by extraction with ether; the ethyl(3-chlorobuten-2-yl)-aniline was isolated by alkalization, dried, and distilled in vacuum. Yield 7.55 g (36%).

B.p. 131-134° (15 mm), d_4^{20} 1.0534, n_D^{20} 1.5570, MR_D 63.9. $C_{12}H_{16}NCl\digamma_4$. Calculated: 62.355.

Found %: Cl 16.71. $C_{12}H_{16}NCl$. Calculated %: Cl 16.90.

4. Alkylation of ethyl acetoacetate with 1,3-dichlorobutene-2 under a variety of conditions is detailed in Tables 1-6.

A special experiment (Table 1) showed that gradual addition of alkali does not modify the results. Experiments were performed along the lines of experiment 3. The reaction mixture was worked up as previously described [1].

In the experiments with 10 N potassium hydroxide (Table 2) the caustic alkali solution was added to the reaction mixture over a period of 20 minutes, after which the heating and stirring were continued for a further 5 minutes. All other experiments were carried out similarly to experiment 3.

Caustic alkali solution was added to the reaction mixture in the course of 20 minutes (Table 3). Heating and stirring were continued for another 5 minutes.

The halide was added to the reaction mixture at the start of the experiment (Table 4), and the caustic alkali solution was added dropwise in the course of 20 minutes. Heating and stirring were continued for another 5 minutes.

Halides were used in 50% of the equimolar quantity in order to ensure complete solubility (Table 5). In all of the experiments 10 ml water was added to the reaction mixture at the start, and 10 ml of 10 N caustic alkali solution was added dropwise over a period of 20 minutes. Heating and stirring were continued for a further 5 minutes.

Dimethyldibenzylammonium chloride was added to the reaction mixture at the start of the experiment; caustic alkali solutions were introduced dropwise in the course of 20 minutes. Heating and stirring were continued for a further 5 minutes.

SUMMARY

1. It is shown that quaternary ammonium bases can serve in place of metallic hydroxides in the alkylation of compounds with a labile hydrogen atom in an aqueous alkaline medium.

2. Interaction of dimethyldibenzylammonium phenate with 1,3-dichlorobutene-2 gives 3-chlorobuten-2-yl-phenyl ether in a yield $3\frac{1}{2}$ times as great as when starting from sodium phenate.

3. Comparison of the results of alkylation of ethyl acetoacetate under the action of lithium, sodium and potassium hydroxides showed that the yields of alkylation products increased with falling basicity.

4. It is shown that the yield of products of alkylation of ethyl acetoacetate rises when halides of the alkali metals are added to the reaction mixture.

5. Dimethyldibenzylammonium phenate was prepared and described for the first time.

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INVESTIGATIONS OF GLYCOL ETHERS

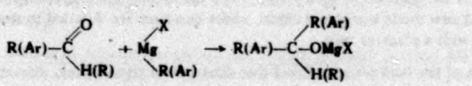
XXX. SYNTHESIS OF ETHERS OF DIMETHYLENEGLYCOL

Shamkhal Mamedov and M.R. Kulibekov

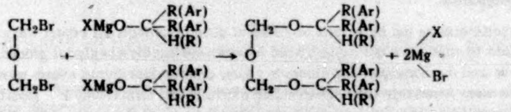
A few representatives of ethers of dimethyleneglycol have been described in the literature [1].

In the present work we attempted to establish whether the organomagnesium synthesis of ethers, previously proposed by one of us [2] for the preparation of methyleneglycol ethers, could be applied to the synthesis of a series of ethers of dimethyleneglycol. It was also intended to study their chemical transformations. These syntheses were realized by the action of *a, a'*-dibromodimethyl ether on the products of interaction of aliphatic, aromatic and heterocyclic aldehydes and ketones with various organomagnesium compounds.

The reaction may be expressed by the equations:



(1)



(2)

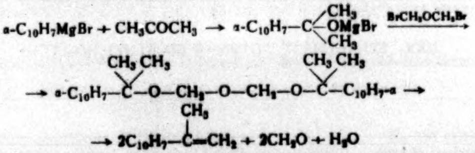
Due to the activity of the bromine in dibromodimethyl ether, the second stage of Reaction (2) goes fairly smoothly and can be completed by gentle heating of the reaction mixture at the boiling point of the solvent (diethyl ether).

No mention of the tertiary dimethyleneglycol ethers could be found in the literature. As our experiments showed, they can be synthesized with facility by the organomagnesium method, starting from ketones and esters. Heterocyclic ethers of dimethyleneglycol have likewise not been described in the literature. These ethers can also be synthesized by the same method, starting from furfural as the aldehydic component of the reaction. Many investigators [3-5] have studied the action of various organomagnesium compounds on furfural. A.G. Chichibabin [3] points out that methylfuryl alcohol is formed when ethyl magnesium iodide acts on furfural.

Our experiments showed that the magnesium-containing furyl alcoholates, resulting from the action of organomagnesium compounds on furfural, undergo severe resinification when treated with *a, a'*-dibromodimethyl ether. This does not occur with the magnesium-containing alcoholates obtained from ordinary aldehydes. Change of temperature of the reaction has no effect, the product being always a badly resinified mass from which it is impossible by any means to isolate the smallest quantity of pure substance. If, however, this reaction is performed in presence of a small quantity of dimethylaniline, resinification is nearly suppressed and the reaction proceeds more or less normally in the direction of synthesis of dimethyleneglycol ethers. We consider the cause of resinification of the reaction products to be the acidic character of *a, a'*-dibromodimethyl ether which leads to polymerization of furfural. A weakly alkaline medium was established, before introduction of *a, a'*-dibromodimethyl ether, by addition of freshly distilled dimethylaniline (25-30% on the weight of bromoether). A normal reaction course was dependent, in addition, on the quality and proportions of the starting components, on the thermal conditions of the reaction, and on the velocity of the furfural.

Further work on the synthesis of dimethyleneglycol ethers revealed that some of the starting halogen derivatives lead to formation of unstable tertiary dimethyleneglycol ethers, which on distillation in vacuo break down to unsaturated hydrocarbon, formaldehyde and water.

The reaction may be expressed by the equations:



$$\alpha\text{-}C_{10}H_7MgBr + CH_3COCH_3 \rightarrow \alpha\text{-}C_{10}H_7{-}C(CH_3)_2{-}OMgBr \xrightarrow{BrCH_2OCH_2Br}$$

$$\rightarrow \alpha\text{-}C_{10}H_7{-}C(CH_3)_2{-}O{-}CH_2{-}O{-}CH_2{-}O{-}C(CH_3)_2{-}C_{10}H_7\text{-}\alpha \rightarrow$$

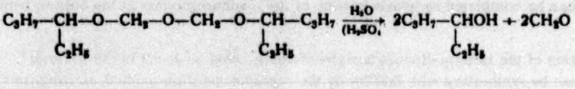
$$\rightarrow 2C_{10}H_7{-}C(CH_3){=}CH_2 + 2CH_2O + H_2O$$

Unsymm. methyl-α-naphthylethylene is here obtained in a yield of 42% calculated on the acetone. A similar picture is obtained on coupling α-naphthyl magnesium bromide with acetaldehyde (with formation of naphthylethylene) and on coupling with butyraldehyde (with formation of symm. ethyl α-naphthylethylene. In the two last cases the yields are 38.5 and 40% respectively.

Nevertheless, in many cases the synthesis of dimethyleneglycol ethers goes without complications, and the corresponding ethers are obtained in good yields. With the help of the organomagnesium method we synthesized and investigated 13 new methyleneglycol ethers, whose constants are detailed in the table. All of the new compounds are liquids with a pleasant odor.

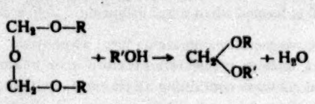
In the course of the work we established that dimethyleneglycol ethers, like the methyleneglycol ethers, are susceptible to hydrolysis and alcoholysis and are very easily decomposed by hydrogen chloride and various organomagnesium compounds.

A series of experiments on the hydrolysis of different dimethyleneglycol ethers was carried out. Hydrolysis is always accompanied by rupture of the oxygen bond between the methyleneglycol groups, which leads to formation of formaldehyde and the corresponding alcohols. Nine dimethyleneglycol ethers were hydrolyzed. The products of hydrolysis were invariably the corresponding alcohols and formaldehyde. Isolation and identification of these alcohols afforded the possibility of establishing the structure of the ethers. The hydrolysis of the ether of dimethyleneglycol with formation of ethylpropyl carbinol may be cited as an example:



$$C_3H_7{-}CH(C_2H_5){-}O{-}CH_2{-}O{-}CH_2{-}O{-}CH(C_2H_5){-}C_3H_7 \xrightarrow[(H_2SO_4)]{H_2O} 2C_3H_7{-}CHOH(C_2H_5) + 2CH_2O$$

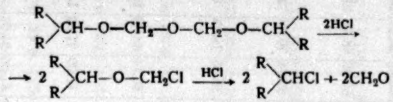
Alcoholysis of these ethers proceeded similarly to their hydrolysis, i.e., with rupture at the oxygen between the two methylene groups. This cleavage always leads to ethers of methyleneglycol:



$$CH_2{-}O{-}R \,|\, O \,|\, CH_2{-}O{-}R + R'OH \rightarrow CH_2\langle^{OR}_{OR'} + H_2O$$

Depending upon the radical of the alcohol taken, the products of alcoholysis can be methyleneglycol ethers of symmetrical or unsymmetrical structure. Alcoholysis is evidently a two-step reaction. Full and partial ethers of methyleneglycol are obtained in the first step, and the partial ether undergoes etherification in the second step.

Hydrogen chloride acts upon dimethyleneglycol ethers in the cold to give α-chloromethyl-alkyl ethers ($R-O-CH_2Cl$); this reaction again indicates the weakness of the oxygen bond between the methylene groups. In these conditions, however, methyleneglycol ethers of secondary alcohols give secondary chlorides and formaldehydes. These chlorides are apparently the products of a subsidiary reaction in which α-chloromethyl-alkyl ethers are formed; the latter are unstable and suffer further chlorination:



Formation of a secondary chloride is consistent with the structure of dimethyleneglycol ethers.

EXPERIMENTAL

1. Synthesis of full ether of dimethyleneglycol with methylbutyl carbinol (table, Compound 1). To the organomagnesium compound obtained from 4.8 g magnesium and 18.5 g butyl chloride was added 8.8 g of acetaldehyde dissolved in an equal volume of absolute ether. After 6 hours 18 g α,α'-dibromodimethyl ether (dissolved in an equal volume of absolute ether) was added. After the bromoether had been added, the reaction flask was heated on a water bath for 3 hours with continuous stirring. The reaction mixture was left overnight. Completion of reaction was marked by the disappearance of the characteristic pungent odor of α,α'-dibromodimethyl ether. The reaction product was decomposed with cold water, and 7.5 g of sec-dihexyl ether of methyleneglycol was isolated in the usual manner. Constants are given in the table (Compound 1).

A further 12 full ethers of dimethyleneglycol were synthesized in similar conditions. Some of their constants are also given in the table.

2. Hydrolysis of the full ether of dimethyleneglycol with isobutyl-n-butyl carbinol was effected by heating 10 g of the ether with 40 ml water containing 2 ml concentrated sulfuric acid for several hours with continuous mechanical stirring. By the usual procedure, 6.0 g of a liquid identifiable as isobutyl-n-butyl carbinol [6] was isolated.

B.p. 180-183°, d_4^{20} 0.8159, n_D^{20} 1.4320; MR_D 45.74; calculated 45.29. Found: M 145.9. $C_9H_{20}O$. Calculated M 144.

Formaldehyde was detected in the aqueous solution after extraction of the reaction product with ether. The structure of these ethers is confirmed by the formation of the corresponding alcohol and of formaldehyde as products of hydrolysis of the synthesized methyleneglycol ethers.

3. Alcoholysis of the full ethyl ether of dimethyleneglycol ($C_2H_5-O-CH_2-O-CH_2-O-C_2H_5$). Alcoholysis of 8.5 g of the ether was effected in the usual manner in 40 g n-butyl alcohol containing 2 ml sulfuric acid. After working up by the normal procedure, 2 g of the dibutyl ether of methylene glycol was obtained.

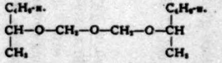
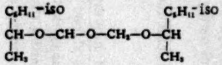
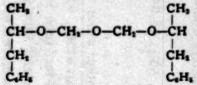
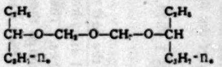
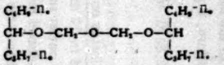
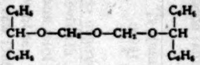
B.p. 68-71° (6 mm), d_4^{20} 0.8392, n_D^{20} 1.4073, MR_D 46.94; calculated 47.05. Found: M 162.7. $C_9H_{20}O_2$. Calculated: M 160.0.

4. Action of hydrogen chloride on the full ethyl ether of dimethylene glycol. 9.5 g of the full ethyl ether of dimethyleneglycol, dissolved in 10 ml anhydrous ether, was placed in a large test tube closed with a cork which was fitted with inlet and outlet tubes. The test tube was cooled with a freezing mixture and a stream of dry hydrogen chloride was introduced through the inlet tube until a strong stream of HCl was discharged from the outlet tube. The product was dried, the ether was driven off, and the residue was fractionated to give 2 g of fuming liquid, identified as α-chloromethyl-ethyl ether [7].

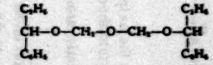
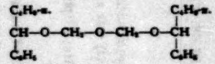
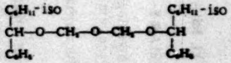
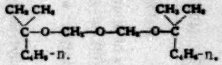
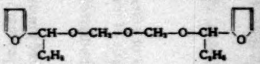
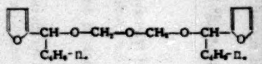
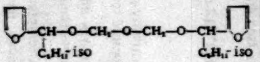
B.p. 78-81°, d_4^{20} 1.0015, n_D^{20} 1.4010, MR_D 22.90; calculated 22.56.

Found %: Cl 38.23. M 93.7. C_3H_7OCl. Calculated %: Cl 37.56. M 94.5.

Dimethyleneglycol Ethers

Compound No.	Structure of ether	Name	Empirical formula	Boiling point	d_4^{20}	n_D^{20}	MR_D		M		% Cl		% H	
							found	calculated	found	calculated	found	calculated	found	calculated
1	 $\underset{CH_3}{\overset{C_4H_9\text{-n.}}{CH}}-O-CH_2-O-CH_2-O-\underset{CH_3}{\overset{C_4H_9\text{-n.}}{CH}}$	Full ether of dimethyleneglycol with methyl-n-butyl carbinol	$C_{14}H_{30}O_3$	111—114° (5 мм)	0.8666	1.4240	72.43	71.78	249.4	246	67.98	68.29	12.31	12.19
2	 $\underset{CH_3}{\overset{C_5H_{11}\text{-iso}}{CH}}-O-CH-O-CH_2-O-\underset{CH_3}{\overset{C_5H_{11}\text{-iso}}{CH}}$	Full ether of dimethyleneglycol with methyl-isoamyl carbinol	$C_{18}H_{34}O_3$	101—103 (3 мм)	0.8466	1.4140	80.87	81.02	271.9	274	69.84	70.07	12.73	12.40
3	 $\underset{\substack{CH_2\\C_6H_5}}{\overset{CH_3}{CH}}-O-CH_2-O-CH_2-O-\underset{\substack{CH_2\\C_6H_5}}{\overset{CH_3}{CH}}$	Full ether of dimethyleneglycol with methyl-benzyl carbinol	$C_{20}H_{26}O_3$	153—155 (5 мм)	0.0538	1.5438	93.48	93.69	311.9	314	76.76	76.43	8.50	8.29
4	 $\underset{C_3H_7\text{-n.}}{\overset{C_2H_5}{CH}}-O-CH_2-O-CH_2-O-\underset{C_3H_7\text{-n.}}{\overset{C_2H_5}{CH}}$	Full ether of dimethyleneglycol with ethyl-n-propyl carbinol	$C_{14}H_{30}O_3$	110—112 (4 мм)	0.8765	1.4262	71.94	71.78	245.3	246	68.14	68.29	12.38	12.18
5	 $\underset{C_3H_7\text{-n.}}{\overset{C_4H_9\text{-n.}}{CH}}-O-CH_2-O-CH_2-O-\underset{C_3H_7\text{-n.}}{\overset{C_4H_9\text{-n.}}{CH}}$	Full ether of dimethyleneglycol with n-propyl-n-butyl carbinol	$C_{18}H_{38}O_3$	117—120 (14 мм)	0.8670	1.4327	90.45	90.25	304.5	302	71.09	71.52	13.01	12.58
6	 $\underset{C_6H_5}{\overset{C_6H_5}{CH}}-O-CH_2-O-CH_2-O-\underset{C_6H_5}{\overset{C_6H_5}{CH}}$	Full ether of dimethyleneglycol with diphenyl carbinol	$C_{28}H_{26}O_2$	T. m.p. 207°	—	—	—	—	408.2	410	81.66	81.95	6.61	6.34

(continued)

Compound No.	Structure of ether	Name	Empirical formula	Boiling point	d_4^{20}	n_D^{20}	MR_D		M		% Cl		% H	
							found	calcu-lated	found	calcu-lated	found	calcu-lated	found	calcu-lated
7		Full ether of dimethyleneglycol with ethyl-phenyl carbinol	$C_{20}H_{26}O_3$	141—143° (5 мм)	1.0550	1.5455	94.12	93.68	316.0	314	75.97	76.43	8.11	8.27
8		Full ether of dimethyleneglycol with n-butyl-phenyl carbinol	$C_{24}H_{34}O_3$	145—148 (3 мм)	1.0307	1.5360	111.87	112.14	367.0	370	77.97	77.83	9.43	9.18
9		Full ether of dimethyleneglycol with isoamyl-phenyl carbinol	$C_{26}H_{38}O_3$	150—153 (5 мм)	1.0015	1.5215	121.09	121.39	395.8	398	77.97	78.39	9.71	9.54
10		Full ether of dimethyleneglycol with dimethyl-n-butyl carbinol	$C_{14}H_{34}O_3$	96—98 (3 мм)	0.8894	1.4350	80.37	81.02	276.0	274	69.69	70.07	12.27	12.40
11		Full ether of dimethyleneglycol with ethyl-furyl carbinol	$C_{16}H_{22}O_5$	127—130 (5 мм)	1.0476	1.4865	80.64	80.43	292.3	294	65.78	65.3	7.94	7.48
12		Full ether of dimethyleneglycol with n-butyl-furyl carbinol	$C_{20}H_{30}O_5$	142—144 (5 мм)	1.0312	1.4958	99.11	98.90	348.2	350	68.04	68.54	8.79	8.57
13		Full ether of dimethyleneglycol with isoamyl-furyl carbinol	$C_{22}H_{34}O_5$	144—146 (4 мм)	1.0289	1.5015	108.30	108.14	374.4	378	69.66	69.84	8.64	8.99

Action of hydrogen chloride upon the full ether of dimethyleneglycol with n-propyl-n-butyl carbinol (table, Compound 5). Conditions were similar to those in the preceding experiment. Starting from 8 g of the dimethyleneglycol ether, 2.5 g of 4-chlorooctane was obtained in the form of a transparent, oily liquid.

B.p. 85-90° (14 mm), d_4^{20} 0.8756, n_D^{20} 1.4290, MR_D 43.68; calculated 44.01. Found M 149.6. $C_8H_{17}Cl$. Calculated M 148.5.

Formation of the above chloro compound is an indication that the action of HCl on dimethyleneglycol ethers is more far-reaching.

5. Synthesis of the full ether of dimethyleneglycol with propyl-*a*-naphthyl carbinol. An organomagnesium compound was prepared from 6 g metallic magnesium and 52 g *a*-bromonaphthalene. The reaction flask was cooled with iced water to prevent formation of dinaphthyl. After 6 hours the reaction product was cooled with a mixture of ice and salt; dropwise addition was then made of 18 g butyraldehyde dissolved in an equal volume of diethyl ether. After 6 hours, 18 g of *a*,*a*'-dibromodimethyl ether diluted with 25 ml absolute ether was slowly run dropwise into the magma of magnesium-containing alcoholate. After the bromoether had been added, the reaction flask was heated on a water bath for 3 hours while stirring. The following day, when the odor of the bromoether had disappeared, dropwise addition was slowly made to the reaction mixture of 50 ml water with cooling and stirring. Two liquid layers were formed. After working up in the usual manner, the liquid was fractionally distilled in vacuo: 1st fraction 98-161° (18 mm), 2.5 g; 2nd 161-164° (18 mm), 8.5 g; residue 2.0 g.

The constants of the second fraction did not correspond to those of the sought-for dimethyleneglycol ether. The product was an oily liquid with a characteristic odor reminiscent of that of petroleum products; it decolorized bromine water and gradually turned yellow in the air.

Closer examination showed that the product is symm. ethyl-*a*-naphthylethylene; yield 40% (on the aldehyde).

B.p. 161-164° (18 mm), d_4^{20} 1.0222, n_D^{20} 1.6218, MR_D 62.70. $C_{14}H_{14}F_6$. Calculated 59.65 (EMR_D + 3.05).

Found %: C 91.98; H 7.73. M 179.9, 184.2. $C_{14}H_{14}$. Calculated %: C 92.39; H 7.69. M 182.0.

For the purpose of synthesis of the full ether of dimethylene glycol and dimethyl-*a*-naphthyl carbinol, the following were charged in succession into a flask: 6 g magnesium, 52 g *a*-bromonaphthalene, 14.5 g acetone and 23 g *a*,*a*'-dibromodimethyl ether. The reaction product (16.5 g) was fractionated in vacuo to give 9 g (42% on the acetone) of unsymm. methyl-naphthylethylene [7].

B.p. 162-164° (30 mm), d_4^{20} 1.0299, n_D^{20} 1.6175, MR_D 57.17. $C_{13}H_{12}F_6$. Calculated 55.03 (EMR_D + 2.04).

An attempt was similarly made to obtain the ether of dimethyleneglycol with methyl-*a*-naphthyl carbinol from 6 g magnesium, 52 g *a*-bromonaphthalene, 11 g acetaldehyde and 23 g *a*,*a*'-dibromodimethyl ether. Fractional distillation of the reaction product gave 10.6 g (38.5%) of naphthylethylene. The product possessed a high degree of unsaturation and turned yellow after long standing in the air with exposure to light.

B.p. 120-123° (12 mm), d_4^{20} 1.0341, n_D^{20} 1.6404 [8], MR_D 53.68. $C_9H_{10}F_6$. Calculated 50.41 (EMR_D 3.27).

SUMMARY

1. The possibility of synthesis of ethers of dimethyleneglycol with the help of the organomagnesium method (previously applied to the synthesis of methyleneglycol ethers) was established.

2. Thirteen new ethers of dimethyleneglycol with aliphatic, aliphatic-aromatic and aliphatic-heterocyclic radicals were synthesized.

3. In the attempted synthesis of dimethyleneglycol ethers of furfural under the conditions of the organomagnesium synthesis, the reaction product undergoes polymerization due to the acidic character of the dibromodimethyl ether. This polymerization is suppressed by adding dimethylaniline to the reaction mixture before addition of the dibromodimethyl ether.

4. Depending upon the structure of the ether, the presence of the naphthyl radical in dimethyleneglycol

ethers can enhance the activity of the α-hydrogen of the ether, thereby rendering the ether so unstable that on fractionation in vacuo it breaks down with formation of unsaturated aromatic hydrocarbons in good yields.

5. Dimethyleneglycol ethers hydrolyze with facility with formation of the corresponding alcohols and formaldehyde.

6. Alcoholysis of dimethyleneglycol ethers leads to formation of methyleneglycol ethers.

7. Hydrogen chloride acts on dimethyleneglycol ethers in the cold to give α-chloromethyl-alkyl ethers, or chlorides of alkanes if the ethers correspond to secondary alcohols.

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UNSATURATED CYCLIC HYDROCARBONS AND THEIR HALOGENATED DERIVATIVES

XXV. INTERACTION OF METHYLCYCLOHEXADIENE-1,3 WITH HEXABROMOETHANE AND QUINOLINE

N.A. Domnin and V.A. Cherkasova

One of us [1] has proposed a mechanism for the transformation of polyhale derivatives of the hexamethylene series into aromatic compounds on heating with quinoline. This mechanism assumes that intermediate products of the transformation are a six-membered ring with conjugated double bonds and perbromates of quinoline. For the purpose of confirming this mechanism we later carried out reactions of cyclohexadiene-1,3 both with hexabromoethane in presence of quinoline and with a series of quinoline perbromates [2-4]. It was established that benzene is present among the products of all of the reactions, i.e., cyclohexadiene-1,3 is partly transformed into benzene in each case under the reaction conditions.

We were interested in establishing whether homologs of cyclohexadiene-1,3 are transformed into an aromatic hydrocarbon in a reaction involving both halogenation and dehalogenation [1, 2, 5]. With this objective, we reacted methylcyclohexadiene-1,3 with symm. tetrabromoethane, isobutylene dibromide and hexabromoethane in presence of quinoline. It might be postulated that the transformation of methylcyclohexadiene-1,3 into toluene would proceed more completely with hexabromoethane, since it is the only one of the three bromo compounds mentioned that does not contain hydrogen (thus, excluding removal of hydrogen bromide by the quinoline) and is richer in bromine, while the formation with it of perbromates of quinoline in accordance with the proposed mechanism should proceed with greater facility than in the case of the other two bromo compounds. We actually found that the light fraction of the products of reaction of methylcyclohexadiene-1,3 with hexabromoethane in quinoline contains about 60% of toluene. These transformations afford indirect confirmation of the first step of our proposed scheme.

EXPERIMENTAL

Methylcyclohexadiene-1,3 was prepared by the action of pulverized potassium hydroxide on a mixture of (probably) two dibromo compounds – 2,3-dibromomethylcyclohexane and 1,2-dibromomethylcyclohexane (the starting substance was methylcyclohexanol-2 which was dehydrated to an unsaturated hydrocarbon which was then brominated). The absence of toluene from the hydrocarbon was verified by spectroscopic (ultraviolet) examination. Hexabromoethane was prepared by the method of G.G. Gustavson [6].

7.8 g methylcyclohexadiene-1,3, 60 g hexabromoethane and 12 g quinoline were refluxed in a small flask on an oil bath for 3 hours, at first at 135° and later at 145-155°. The contents of the flask stratified during the operation, and a characteristic crackling was heard. The lower layer was very viscous and nearly black, and it solidified on cooling. The upper layer was a brown, mobile liquid from which a fraction up to 170° was distilled off (first drops at 108° were transparent, the remainder was cloudy). Weight 21.7 g. The product was washed with dilute sulfuric acid and water, dried over magnesium sulfate, and distilled to give a fraction boiling at 108-116° (6.2 g). After numerous distillations and dryings both over metallic sodium and potassium hydroxide, a 109-111.5° fraction was collected that still contained traces of bromine (Beilstein test), this fact being also reflected in its density ($d_4^{18.5}$ 1.0082, $n_D^{18.5}$ 1.4889). It refracted light strongly and decolorized a weak solution of potassium permanganate. The bromine number, determined by the McIlhiney method [7], was 75 (the bromine number theoretically calculated for methylcyclohexadiene-1,3 is 170). On the basis of the bromine number the reaction product contained 56% of toluene. The absorption curve of an alcoholic solution of the reaction product was plotted with the SF-11 spectrophotometer [8]. These measurements indicated a toluene content of 60-63%. Results obtained with the other aliphatic bromo compounds are not cited here because the conditions employed were essentially the same as with hexabromoethane, but the yields of toluene were lower.

SUMMARY

Interaction of methylcyclohexadiene-1,3 with hexabromoethane and quinoline leads to transformation of methylcyclohexadiene-1,3 into toluene. The content of the latter in the reaction product is about 60%.

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*Original Russian pagination. See C.B. translation.

THE PROBLEM OF THE ELECTRONIC STRUCTURE AND REACTIVITY OF FREE RADICALS

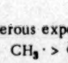
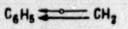
V.V. Razumovsky

On the basis of numerous experimental investigations the following order of activity of free radicals is proposed at the present time: $CH_3\cdot > C_2H_5\cdot > n\text{-}C_3H_7\cdot > iso\text{-}C_3H_7\cdot > sec\text{-}C_4H_9\cdot > CH_2{=}CH{-}CH_2\cdot > CH_3{-}CH{=}CH{-}CH_2\cdot$; $C_6H_5CH_2\cdot > (C_6H_5)_2CH\cdot > (C_6H_5)_3C\cdot$.

What explanation can be found for this order of activity?

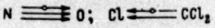
The electronegativity of the carbon atoms in organic molecules decreases regularly in the order: $H_3C^{---} > H_2C^{--} > HC^{-}$.

The differences in reactivity of the electrons of the C–C and C–H bonds with nuclei of primary, secondary and tertiary carbon atoms leads to differing polarity of the individual portions of the organic molecule, to a change in the character of the bond between the individual carbon and hydrogen atoms in hydrocarbon chains and rings. Methine groups in organic molecules are more strongly polarized than methylene groups, and the latter in turn are more strongly polarized than methyl groups. These conclusions from the theory of electronic tautomerism, which have been disputed for 30 years, have been confirmed in recent years [1].

The methyl radical  has a high activity because its carbon atom possesses a higher degree of electronegativity than the carbon atoms of other alkyl radicals. The energy of interaction of the "free" electron with the nucleus of the carbon atom is therefore the lowest in the methyl radical, and its reactivity is accordingly the highest. In the propyl radical the "free" electron is located at the secondary carbon atom, while in the isopropyl radical it is at the tertiary carbon. Consequently, in the latter radical the energy of interaction of the "free" electron with the nucleus of the carbon atom is considerably higher than in the n-propyl, and the isopropyl radical is bound to have a low activity. In the allyl radical the interaction of the "free" electron with the nucleus of the tertiary carbon atom leads to increased release of energy which affords the opportunity to the "free" electron to take up an energetically more advantageous position. This also accounts for the very low relative activity of the allyl radical [2, 3]. The extremely low activity of the benzyl radical, established by G.A. Razuvaev and Yu.A. Oldekop [4], is due to the "free" electron having a longer residence period at the quaternary carbon atom of the benzene ring, i.e., the electron is, as it were, drawn into the benzene ring: 

Interaction of the free electron with the nucleus of a quaternary carbon is considerably more intensive than with the nucleus of a tertiary carbon atom. There is a corresponding fall in the store of energy of the "free" electron and of the activity of the benzyl radical in comparison with the allyl radical.

In terms of the concepts of electronic tautomerism, the extremely low activity of free radicals of the type of $\cdot CCl_3$ and $\cdot NO$ [5] is due to the considerably longer residence time of the "free" electron at the atoms with increased affinity towards it (the oxygen atom or the three chlorine atoms):



Interaction of the "free" electron with the nucleus of such an acceptor atom governs the increased release of energy, and accounts for the marked drop in activity of the radical.

Heterolytic rupture of the bonds in a molecule can lead to formation of radicals with two unshared electrons, i.e., ions of $(C_6H_5)_2\ddot{C}H$, $(C_6H_5)_3\ddot{C}$, $(C_6H_5{-}C_6H_4)_3\ddot{C}$.

The relative activity of such types of ions is governed by the residence time of the two "free" electrons at the atomic nucleus of the reaction center of the radical, and consequently by the energy of interaction of these electrons with the nucleus. In the case of tribiphenylmethyl, which contains a large number of quaternary carbons, the energy of interaction of the "free" (unshared) electrons with the nucleus of its central atom governs the very high stability of the radical. In diphenylmethyl the "free" electrons have a longer residence time at the carbon atom of the methine group, whereas in triphenylmethyl the "free" electrons are preferentially located at the quaternary carbon. Consequently, in these two cases the energy of interaction of the "free" electrons with the nucleus determines the considerably higher relative activity of diphenylmethyl [6].

As we see, the order of activity of free radicals follows from the concepts of electronic tautomerism [7]. Ideas about the polarity of free radicals have been expounded in recent years in a number of papers in connection with the interpretation of the reactivity of such radicals [2]. But as far back as 1932 we correlated the activity of free radicals with their polarity. Some contemporary workers in the field of free-radical chemistry are using, it should be noted, a terminology similar to that used by us in the first communications on this theme. In papers published in 1932-1939 we regarded the lowering of activity of free radicals as an increase of the "degree of dubleting of free electrons." By this term we implied the different character and different energy of activation of electrons and atomic nuclei within the molecule [8].

In 1955 B.A. Dolgoplosk and his coworkers wrote: "The alteration of the electronic structure of a free radical resulting from the inductive positive influence of alkyl groups can be regarded as a special case of fall in "the degree of unpairedness" of the unshared electron of the free radical" [2]. The different "degree of unpairedness" ("degree of dubleting") of the unshared electron of the free radical depends upon the residence time of this electron in the field of the atom ("reaction center") of the free radical and upon the intensity of its interaction with the nucleus of that atom.

In recent years N.N. Semenov has used the concept of the pulling of the "free" electron into the interior of the molecule to account for the lowering of activity of radicals. He writes: "According to the theory here developed, a specific role in the chemical kinetics is played by the energy of interaction of the "free" electron with the remaining bonds of complex radicals" [3].

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HETEROCYCLIC COMPOUNDS

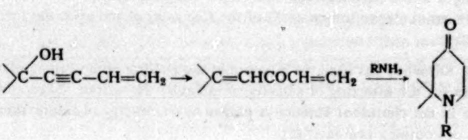
56. THE ACTION OF PRIMARY AMINES UPON PROPENYLISOPROPENYL KETONE

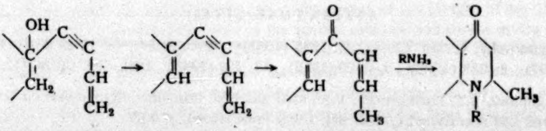
I.N. Nazarov and N.I. Shvetsov

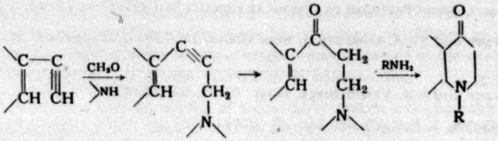
γ-Piperidones are important starting substances for the synthesis of physiologically active compounds, and in particular of anesthetics.

In the past, however, the number of methods available for their preparation was limited, and they were employed for the synthesis of γ-piperidones of only one specific type. γ-Piperidones containing different alkyl substituents in the piperidine ring were especially inaccessible, and these are of the greatest interest for synthesis of highly active analgesics.

Important possibilities in the field of synthesis of γ-piperidones with diverse structures were opened up after the discovery in our laboratory of new methods of their preparation on the basis of acetylene derivatives.







One of the most interesting methods of preparation of γ-piperidones is based on the interaction of ammonia or primary amines with vinyl-propenyl ketones formed by hydration of divinylacetylenic hydrocarbons in aqueous methanolic solutions [1]. We employed this method for the preparation of diverse 1-alkyl-2,5-dimethyl-4-piperidones (II) that were required for the synthesis of homologs of Promedol* and Isopromedol* with different alkyl substituents at the nitrogen of the piperidine ring. All of the 1-alkyl-2,5-dimethyl-4-piperidones described in the present communication were obtained on the basis of the commercially available dimethylvinylethynyl carbinol according to the scheme:

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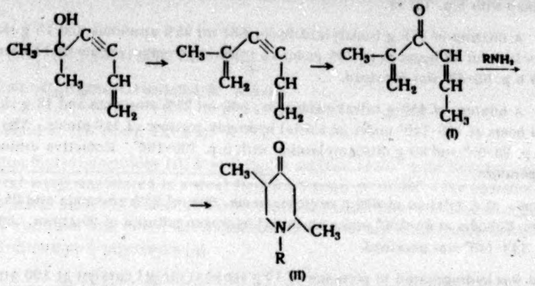
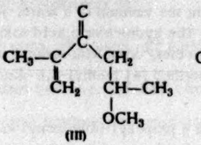
*Russian trade name.

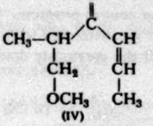


R = C_2H_5, C_3H_7, iso-C_3H_7, C_3H_5, C_4H_9, iso-C_4H_9, iso-C_5H_{11}, cyclo-C_6H_{11}

Interaction of propenyl-isopropenyl ketone (I) with higher primary aliphatic amines also proceeds as smoothly as with methylamine [2], and leads to 1-alkyl-2,5-dimethyl-4-piperidones (II) in a yield of 70-80%. Methoxyketones (III-V) can also be used for the preparation of 1-alkyl-2,5-dimethyl-4-piperidones. These ketones are obtained by addition of methanol to propenyl-isopropenyl ketone. The reaction of methoxyketones (III-V) with primary amines must be carried out, however, in presence of water. Replacement of propenyl-isopropenyl ketone by methoxyketones (III-V) in the reaction with cyclohexylamine leads to a fall in yield of 1-cyclohexyl-2,5-dimethyl-4-piperidone from 50 to 15%.



(III)



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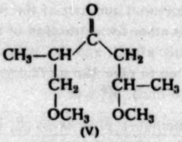

(V)

Apart from propylamine, the primary amines used in the present work were obtained in yields of 31-76% by hydrogenation of aldehydes and ketones with Ni catalyst in presence of ammonia (reductive amination [3]) $>C{=}O \xrightarrow[\text{Ni}]{H_2,\ NH_3} >CHNH_2$.

The 1-alkyl-2,5-dimethyl-4-piperidones here described will be used for the synthesis of 1-alkyl-2,5-dimethyl-4-phenyl-4-piperidols and their esters (homologs of Promedol and Isopromedol) with the objective of comparing their pharmacological properties.

EXPERIMENTAL

Ethylamine. To 570 g acetaldehyde, cooled to −10°, was added 900 ml 25% aqueous ammonia, followed by 18 g skeletal nickel catalyst. The mixture was heated in a steel autoclave for 14 hours at 60-90° under an initial hydrogen pressure of 100 atmos. The resultant solution was decanted from the catalyst, acidified with concentrated hydrochloric acid, evaporated nearly to dryness in vacuo, and treated with 50% potassium hydroxide solution (with cooling). Fractional distillation of the separated oil gave 178 g (31%) of ethylamine with b.p. 17-22°. Reductive amination of other aldehydes and ketones was performed in similar fashion.

Isopropylamine. 580 g acetone and 800 ml 25% ammonia solution were hydrogenated in presence of 18 g skeletal nickel catalyst for 8 hours at 60-80° under an initial hydrogen pressure of 110 atmos. The mixture was worked up on the lines described above and gave 439 g (76%) isopropylamine with b.p. 32-34°.

n-Butylamine. A mixture of 600 g n-butyraldehyde and 800 ml 25% ammonia was heated for 11 hours at

70-90° in presence of skeletal nickel catalyst under an initial hydrogen pressure of 110 atmos. 450 g (75%) of n-butylamine was obtained with b.p. 76-78°.

Isobutylamine. A mixture of 475 g isobutyraldehyde, 680 ml 25% ammonia and 15 g skeletal nickel was heated in a steel autoclave for 12 hours at 60-90° under an initial hydrogen pressure of 110 atmos. 283 g (65%) of isobutylamine with b.p. 66-68° was obtained.

Isoamylamine. A mixture of 450 g isovaleraldehyde, 500 ml 25% ammonia and 15 g skeletal nickel catalyst was heated for 12 hours at 130-140° under an initial hydrogen pressure of 110 atmos. The reaction gave 240 g isoamylamine with b.p. 93-95° and 39 g diisoamylamine with b.p. 180-190°. Reductive amination does not take place at a lower temperature.

Cyclohexylamine. a) A mixture of 800 g cyclohexanone, 600 ml 25% ammonia and 25 g skeletal nickel catalyst was heated for 12 hours at 80-100° under an initial hydrogen pressure of 90 atmos. 698 g (87%) of cyclohexylamine with b.p. 143-145° was obtained.

b) 275 g aniline was hydrogenated in presence of 10 g skeletal nickel catalyst at 100 atmos for 11 hours at 145-155°. Repeated fractional distillation gave 92 g of cyclohexylamine with b.p. 142-145°. Higher fractions (weight 25 g) with b.p. 150-170° and the distillation residue (150 g) are dicyclohexylamine and tricyclohexylamine.

n-Propylamine. 720 g acrylonitrile was hydrogenated in presence of 10 g skeletal nickel catalyst at 120 atmos for 2 hours at room temperature and for 3 hours at 100-110°. Numerous fractional distillations gave 260 g of propylamine with b.p. 49-50° and 490 g of a mixture of amines with b.p. 50-140° containing dipropyl- and tripropylamines.

1-Ethyl-2,5-dimethyl-4-piperidone (II, R = C_2H_5). 168 g methoxyketone (III-V) (b.p. 50-69° at 10 mm), obtained by hydration of vinylisopropenylacetylene, 60 g ethylamine and 50 ml water were heated for 5 hours in a steel ampoule. The contents of the vessel were then transferred to a flask, and acidified with concentrated hydrochloric acid; the methanol and part of the water were driven off in the vacuum of a water-jet pump, and the residue was treated with ether for extraction of the neutral products. The hydrochloric acid solution of the bases was saturated with caustic alkali, and the product was extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo to give 128 g (72.1%) of the previously described [4] 1-ethyl-2,5-dimethyl-4-piperidone with b.p. 76-78° (6 mm), n_D^{20} 1.4630.

1-Propyl-2,5-dimethyl-4-piperidone (II, R = C_3H_7). a) To 225 g propenyl-isopropenyl ketone (b.p. 47-50° at 12 mm) was gradually added (with cooling and stirring) 120 g propylamine, and the mixture was left overnight. The next day the solution was heated for 4 hours at 60°, acidified with 150 ml concentrated hydrochloric acid, and twice extracted with ether for removal of the neutral products. In this manner 15 g of the original propenyl isopropenyl ketone with b.p. 47-50° (12 mm) was separated. The hydrochloric acid solution of the bases was saturated with caustic alkali, and the oil obtained was extracted with ether, dried with sodium sulfate and fractionated in vacuo to give 247 g of 1-propyl-2,5-dimethyl-4-piperidone.

B.p. 80-82° (5 mm), n_D^{20} 1.4602, d_{20}^{20} 0.9260, MR_D 50.01; calculated 50.13.
Found %: N 8.10, 7.85. $C_{10}H_{19}ON$. Calculated %: N 8.29.

The picrate melted at 157-158° (from alcohol).

b) A mixture of 710 g methoxyketones (III-V), 295 g propylamine and 150 ml water was heated in a steel flask for 5 hours at 80°. The reaction mass was acidified with hydrochloric acid, evaporated in vacuo, extracted with ether, and dried with solid sodium hydroxide. The resultant oil was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo. Yield 490 g of 1-propyl-2,5-dimethyl-4-piperidone with b.p. 80-82° (5 mm). The residue in the distillation flask weighed 110 g. 60 g methoxyketones and 30 g propylamine did not enter into reaction.

1-Isopropyl-2,5-dimethyl-4-piperidone (II, R = iso-C_3H_7). A mixture of 280 g methoxyketones (III-V), 120 g isopropylamine and 60 ml water was heated for 5 hours in a steel flask at 70-80°. The reaction mass was then transferred to a round-bottomed flask, acidified with concentrated hydrochloric acid, and evaporated in vacuo. The residue was extracted with ether and saturated with caustic alkali. The resultant base was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo to give 283 g of 1-isopropyl-2,5-dimethyl-4-piperidone.

B.p. 86-87° (8 mm), n_D^{20} 1.4635, d_{20}^{20} 0.9342, MR$_D$ 49.87; calculated 50.13.

Found %: N 8.00. $C_{10}H_{19}ON$. Calculated %: N 8.29.

The picrate melted at 168° (from alcohol).

1-Butyl-2,5-dimethyl-4-piperidone (II, R = C_4H_9). A mixture of 450 g methoxyketones (III-V), 200 g butylamine and 100 ml water was heated in a steel flask for 5 hours at 70-80°. The reaction mass was thereupon acidified with hydrochloric acid, evaporated in vacuo, extracted with ether, and saturated with caustic alkali. The resultant oil was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo to give 292 g of 1-butyl-2,5-dimethyl-4-piperidone [5].

B.p. 75-76° (2 mm), n_D^{20} 1.4630, d_{20}^{20} 0.9258, MR$_D$ 54.53; calculated 54.75.

The picrate melted at 135-136° (from alcohol)

The residue in the distillation flask weighed 120 g. From the neutral products was isolated 140 g of original methoxyketones with b.p. 60-70° (10 mm).

1-Isobutyl-2,5-dimethyl-4-piperidone (II, R = iso-C_4H_9). A mixture of 450 g methoxyketones (III-V), 200 g isobutylamine and 100 ml water was heated for 4½ hours at 70-80°. The reaction mass was acidified with concentrated hydrochloric acid (200 ml), the neutral products were extracted with ether, and the acid solution was evaporated to dryness. The residue from the latter was saturated with caustic alkali, and the resultant product was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuum to give 225 g of 1-isobutyl-2,5-dimethyl-4-piperidone [5].

B.p. 80° (3.5 mm), n_D^{20} 1.4605, d_{20}^{20} 0.9170, MR$_D$ 54.79; calculated 54.75.

The methiodide had m.p. 147-148° (from alcohol).

From the neutral products were recovered 45 g of the original methoxyketones with b.p. 60-65° (10 mm).

1-Isoamyl-2,5-dimethyl-4-piperidone (II, R = iso-C_5H_{11}). A mixture of 185 g isoamylamine, 360 g methoxyketones (III-V), 100 ml water and 250 ml methanol was heated for 5 hours at 80°. The reaction mass was thereupon acidified with 200 ml concentrated hydrochloric acid, the methanol was taken off in vacuo, and the residue was twice extracted with ether and saturated with caustic alkali. The separated oil was dried with sodium sulfate and fractionally distilled in vacuo to give 360 g 1-isoamyl-2,5-dimethyl-4-piperidone [5].

B.p. 90-92° (2 mm), n_D^{20} 1.4615, d_4^{20} 0.9102, MR$_D$ 59.46; calculated 59.36.

The picrate melted at 142.5-143° (from alcohol).

The residue in the distillation flask weighed 25 g. From the neutral products was obtained 22 g of original methoxyketones with b.p. 60-65° (10 mm).

1-Cyclohexyl-2,5-dimethyl-4-piperidone (II, R = cyclo-C_6H_{11}). a) A mixture of 106 g propenyl-isopropenyl ketone, 96 g cyclohexylamine, 50 ml methanol and 50 ml water was heated on a boiling water bath for 5 hours. The reaction solution was then acidified with 100 ml concentrated hydrochloric acid, the methanol was taken off in vacuo, and the residue was twice extracted with ether and treated with 200 ml 25% ammonia. This treatment resulted in separation of 115 g of crystals of 1-cyclohexyl-2,5-dimethyl-4-piperidone with m.p. 73-74° (from gasoline). The filtrate after separation of the crystals was extracted with ether to give an additional crop of 16 g 1-cyclohexyl-2,5-dimethyl-4-piperidone with b.p. 123-132° (4 mm), from which was isolated (via the hydrochloride) 12 g of pure substance with m.p. 73-74°. The total yield from 106 g propenyl-isopropenyl ketone was 127 g (63%) of crystalline 1-cyclohexyl-2,5-dimethyl-4-piperidone [5] with m.p. 73-74°. The hydrochloride melts at 170-171°.

b) A mixture of 29 g methoxyketones (III-V) (b.p. 50-80° at 10 mm), 20 g cyclohexylamine and 5 ml water was heated for 5 hours at 78-82°. The reaction mass was acidified with 50 ml concentrated hydrochloric acid, extracted with ether, and saturated with solid potassium hydroxide. The separated base was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo to give the following fractions: 1st, b.p. 20-70° (15 mm), 3 g; 2nd, b.p. 50-102° (3 mm) 2 g; 3rd, b.p. 105-125° (3 mm), 7.5 g. Residue in flask 15 g. On prolonged standing the 3rd fraction deposited 1.5 g of crystals of 1-cyclohexyl-2,5-dimethyl-4-piperidone with m.p. 73-74°. From the ethereal extract of the neutral products was isolated 6 g of the original methoxyketones with b.p. 50-80° (10 mm).

SUMMARY

Reaction of primary amines with propenyl-isopropenyl ketone or its corresponding β-methoxyketones gave good yields (70-80%) of 1-alkyl-2,5-dimethyl-4-piperidones.

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INVESTIGATION ON OXIDO COMPOUNDS

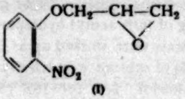
VIII. INTERACTION OF α-OXIDES OF ALLYL ETHERS OF o-, m- AND p-NITROPHENOLS WITH DIETHYLAMINE

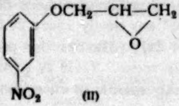
I.I. Chizhevskaya and V.I. Pansevich-Kolyada

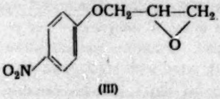
Glycide ethers (α-oxides of allyl ethers) of nitrophenols are mentioned in the literature [1]. They were obtained by interaction of epichlorohydrin with the corresponding phenates. Reactions of these compounds with various components (including some primary amines) have also been investigated. No study has previously been made, however, of the reaction of glycide ethers of nitrophenols with diethylamine. Since some derivatives of glycide ethers of phenols are known to be physiologically active [1], it appeared desirable to extend our knowledge of these substances.

In the present work we synthesized the α-oxides of allyl ethers of o-, m- and p-nitrophenols and studied their reactions with diethylamine.

Allyl ethers of all of the three nitrophenols were prepared by the Claisen reaction [2, 3]. We oxidized these ethers with acetyl hydroperoxide in ethyl ether and obtained the corresponding epoxides: o-, m- and p-1-nitrophenoxy-2,3-epoxypropanes (I, II and III).

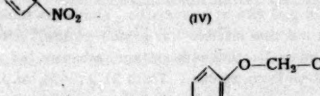

(I)


(II)


(III)

Oxidation takes place slowly; heat is not developed when the hydroperoxide is added, and the process is complete in 10-15 days.

Reaction of the α-oxides of allyl ethers of nitrophenols (I, II, III) with diethylamine was effected by heating the components on a water bath. The reaction products – 1-o-nitrophenoxy-3-diethylaminopropanol-2 (IV), 1-m-nitrophenoxy-3-diethylaminopropanol-2 (V), and 1-p-nitrophenoxy-3-diethylaminopropanol-2 (VI) – are oily liquids that do not distill without decomposition. They react with facility with hydrogen chloride and ethyl iodide to form crystalline hydrochlorides and ethiodides, which are readily soluble in alcohol and water.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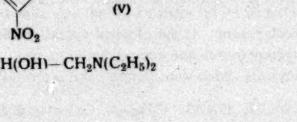
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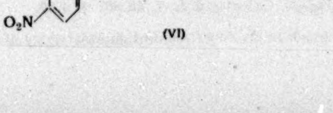
(VI)

According to the literature [4-6], the reaction of the α-oxide of a phenyl allyl ether with dimethylamine proceeds with formation of a secondary aminoalcohol – 1-phenoxy-3-dimethylaminopropanol-2 – whose structure was confirmed by carrying out the reaction in reverse. A product of similar structure is obtained by reacting aniline with the same glycidyl ether of phenol. Addition of ammonia and amines to glycidyl ethers of nitrophenols [1] and to ethers of glycidol [7-14] proceeds in similar fashion.

On the basis of the investigations cited, we can assume that the addition of diethylamine to α-oxides of allyl ethers of o-, m- and p-nitrophenols proceeds similarly under our conditions and that the structure of the reaction products can be represented by formulas IV, V and VI.

The amino derivatives of glycidyl ethers of nitrophenols that we synthesized (IV and VI) were tested pharmacologically*; they were found to be active vasodilatory agents with prolonged action.

EXPERIMENTAL

Allyl ethers of o-, m- and p-nitrophenols were prepared by heating nitrophenols with allyl bromide and potassium carbonate in acetone [2, 3].

Allyl o-nitrophenyl ether. Yield 82% reckoned on the nitrophenol. B.p. 155° (12 mm).

Found %: C 59.97; H 4.87. $C_9H_9O_3N$. Calculated %: C 60.33; H 5.03.

Allyl m-nitrophenyl ether. Yield 89.4%. B.p. 140-141° (6 mm); m.p. 36.2°.

Found %: C 60.48; H 4.96. $C_9H_9O_3N$. Calculated %: C 60.33; H 5.03.

Allyl p-nitrophenyl ether. Yield 67.9%. B.p. 150-151° (6 mm); m.p. 18.2°.

Found %: C 60.53; H 5.24. $C_9H_9O_3N$. Calculated %: C 60.33; H 5.03.

1. Oxidation of Allyl Ethers of Nitrophenols with Acetyl Hydroperoxide

Preparation of 1-o-nitrophenoxy-2,3-epoxypropane (I) (glycidyl o-nitrophenyl ether). To 44 g allyl o-nitrophenyl ether in 50 ml anhydrous ether at 20-23° was slowly added 20.5 g of 90% acetyl hydroperoxide. No heat was developed. Oxidation was complete in 14 days. The reaction products were worked up as in the preceding paper [15], dried with $MgSO_4$ and distilled in vacuo. Yield 22 g (49%) of substance which crystallized in the form of yellowish-white, rhombic crystals, readily soluble in ether and alcohol. B.p. 160-168° (5 mm), m.p. 51-52°.

Found %: C 55.59; H 4.28. $C_9H_9O_4N$. Calculated %: C 55.35; H 4.65.

Preparation of 2-m-nitrophenoxy-2,3-epoxypropane (II) (glycidyl m-nitrophenyl ether). To 20 g allyl m-nitrophenyl ether in 40 ml ether at 20-24° was added 11 g of 88% hydroperoxide. Oxidation was complete after 10 days. At the end of the reaction the mixture had a golden-yellow color. Neutralization of the acetic acid with sodium carbonate brought down light-yellow crystals. Recrystallization from ligroin gave 17.2 g (78%) of substance. M.p. 62-64°.

Found %: C 55.62; H 4.25. $C_9H_9O_4N$. Calculated %: C 55.35; H 4.65.

Preparation of 1-p-nitrophenoxy-2,3-epoxypropane (III) (glycidyl p-nitrophenyl ether). To 38 g of allyl ether of p-nitrophenol in 30 ml ether at 20-24° was added 19 g of 88% hydroperoxide. Oxidation took place slowly without heat development. At the close of oxidation the reaction mixture was golden-yellow. After 10 days the whole of the hydroperoxide had entered into reaction. Neutralization with sodium carbonate led to separation of yellowish crystals which were filtered and recrystallized from ligroin. Yield 21 g (54%), m.p. 67°.

Found %: C 55.25; H 4.21. $C_9H_9O_4N$. Calculated %: C 55.35; H 4.65.

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*Tests were performed by L.A. Yakimovich in the department of pharmacology of the Minsk Medical Institute.

2. Interaction of α-oxides of Allyl Ethers of o-, m- and p-Nitrophenols with Diethylamine

Preparation of 1-o-nitrophenoxy-3-diethylaminopropanol-2 (IV). 10 g of 1-o-nitrophenoxy-2,3-epoxypropane (I) and 12.5 g of diethylamine were refluxed in a flask on a boiling water bath. After 2½ hours, the contents of the flask were mixed with ether and repeatedly washed with water to remove the unreacted diethylamine. The ethereal solution was dried with $MgSO_4$ and the ether was driven off in vacuum. An attempt to distill the reaction product in vacuo led to decomposition. Passage of hydrogen chloride into the ethereal solution of the reaction product gave the hydrochloride in the form of a white, crystalline powder. After recrystallization from alcohol it melted at 219-220°.

Found %: N 8.95; Cl 11.89, 11.86. $C_{13}H_{21}O_4N_2Cl$. Calculated %: N 9.19; Cl 11.64.

Heating of molar proportions of 1-o-nitrophenoxy-3-diethylaminopropanol-2 and ethyl iodide gave the ethiodide in the form of a white crystalline powder with m.p. 134°.

Preparation of 1-m-nitrophenoxy-3-diethylaminopropanol-2 (V). 10 g of 1-m-nitrophenoxy-2,3-epoxypropane (II) and 12.5 g diethylamine were heated on a water bath at 65-70° for 2½ hours. The product was worked up as in the preceding experiment and converted to the hydrochloride and ethiodide. After recrystallization from alcohol the hydrochloride melted at 167-167.5°.

Found %: N 8.84, 9.06. $C_{13}H_{21}O_4N_2Cl$. Calculated %: N 9.19.

After recrystallization from alcohol and ether the ethiodide melted at 190-190.5°.

Preparation of 1-p-nitrophenoxy-3-diethylaminopropanol-2 (VI). 6 g of 1-p-nitrophenoxy-2,3-epoxypropane (III) and 7.5 g of diethylamine were heated on a water bath for 2 hours. The reaction products were worked up by the method described above. The hydrochloride is a white crystalline powder, m.p. 162-165°.

Found %: N 9.13; Cl 11.71, 11.29. $C_{13}H_{21}O_4N_2Cl$. Calculated %: N 9.19; Cl 11.64.

The ethiodide melted at 186-187° after recrystallization from a mixture of alcohol and ether.

SUMMARY

1. Oxidation of allyl ethers of o-, m- and p-nitrophenols with acetyl hydroperoxide gave the epoxides: 1-o-nitrophenoxy-2,3-epoxypropane, 1-m-nitrophenoxy-2,3-epoxypropane, and 1-p-nitrophenoxy-2,3-epoxypropane.

2. α-Oxides of allyl ethers of o-, m- and p-nitrophenols readily enter into reaction with diethylamine with formation of the corresponding aminoalcohol-ethers: 1-o-nitrophenoxy-3-diethylaminopropanol-2, 1-m-nitrophenoxy-3-diethylaminopropanol-2, and 1-p-nitrophenoxy-3-diethylaminopropanol-2.

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INVESTIGATIONS OF UNSYMMETRICAL ORGANIC α-OXIDES

XIV. TRANSFORMATIONS OF PIPERYLENE MONOXIDE

F.G. Ponomarev, O.G. Kharenko and M.F. Shavkova

The chemical properties of piperylene oxides have not previously been studied.* Only one paper has been published on its synthesis [1, 2]. We undertook a systematic investigation in this direction. In the present paper we describe the results of experiments on isomerization and hydration of 2,3-epoxypentene-4 (I) and its condensation with acetone, methanol and diethylamine. We prepared (I) from piperylene via the chlorohydrin.

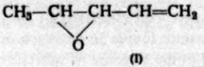
The action of monochlorourea on piperylene might be expected to yield, just like the reaction with bleaching powder [2], the three isomeric chlorohydrins (II), (III) and (IV).

$$\underset{\text{(II)}}{CH_3-CHOH-CHCl-CH{=}CH_2} \quad \underset{\text{(III)}}{CH_3-CH{=}CH-CHOH-CH_2Cl}$$

$$\underset{\text{(IV)}}{CH_3-CHOH-CH{=}CH-CH_2Cl}$$

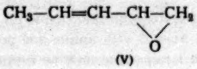
Experiments gave isomers (II) and (III), which were isolated in the pure form and were converted into the corresponding oxides: 2,3-epoxypentene-4 (I) and 1,2-epoxypentene-3 (V).

These syntheses also confirmed the structure of chlorohydrins (II) and (III).



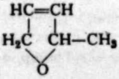
$$CH_3-\underbrace{CH-CH}_{O}-CH{=}CH_2$$

(I)



$$CH_3-CH{=}CH-\underbrace{CH-CH_2}_{O}$$

(V)



(A)

Concerning chlorohydrin (IV), it could not be isolated in the pure form even after numerous fractional distillations, although its quantity was 59% of the total chlorohydrins. An attempt to prepare 2-methyl-α-3,4-dihydrofuran (A) from substance (IV) by heating with concentrated caustic alkali on a boiling water bath was unsuccessful. Chlorohydrin (IV) evidently reacts with alkali in such a manner that other products (which we did not investigate) are formed.

In presence of 1% H_2SO_4, piperylene oxide (I) combines with a molecule of water to form penten-4-diol-2,3 (VI) in 16% yield.

$$\text{(I)} \xrightarrow{1\%\,H_2SO_4} \underset{\text{(VI)}}{CH_3-CHOH-CHOH-CH{=}CH_2}$$

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* A paper just published by Pudovik and Ivanov [7] describes reactions of piperylene oxide with water, acetic anhydride, acetyl chloride and ethyl alcohol.

The structure of glycol (VI) follows from the method of its preparation.

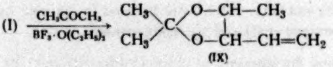
Theoretically, the isomerization of oxide (I) could give two ketones (VII) and (VIII).

$$\underset{(VII)}{CH_3-CO-CH_2-CH=CH_2} \qquad \underset{(VIII)}{CH_3-CH_2-CO-CH=CH_2}$$

We know from the literature that in the event of rearrangement of $\underset{\diagdown O \diagup}{CH_3-CH-CH-CH_2-CH_3}$ and other oxides of the type of $\underset{\diagdown O \diagup}{R-CH-CH-R'}$, where both radicals are aliphatic, the oxide ring is generally cleaved at the carbon atom nearest to the middle of the chain, so that in the ketones formed by isomerization the carbonyl group will always be nearer to the end of the chain [3]. Many examples are also known of rearrangements of olefin oxides in which the oxide ring is broken in the first instance at the carbon atom bound to the vinyl group [4]. It is therefore highly probable that the isomerization of piperylene oxide (I) under the action of Al_2O_3 at 350° results in our case also in the oxide ring being preferentially ruptured from the side of the vinyl group; this leads to formation of penten-1-one-4 (VII) as the main product. The correctness of this mechanism is confirmed by the fact that the isomerizate gave iodoform on treatment with iodine and potassium iodide in presence of sodium hydroxide. This reaction is, of course, characteristic of ketones whose molecule contains the CH_3CO group.

Ketone (VII), possibly contaminated with (VIII), was isolated as the semicarbazone.

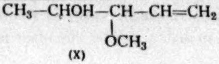
Reaction with acetone of the same oxide (I) in presence of boron fluoride etherate as catalyst gave a 17% yield of 2,2,5-trimethyl-4-vinyldioxolane (IX), whose structure was confirmed by hydrolysis with 5% H_2SO_4 to acetone and penten-4-diol-2,3 (VI).



(IX)

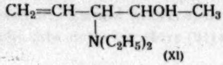
Under the action of boron fluoride etherate, oxide (I) reacts with methanol in the cold with formation of pentenediol methyl ether. When treated with iodine and potassium iodide in presence of sodium hydroxide, the ether readily gives iodoform; the latter could only be formed at the expense of substance (X) whose molecule contains the CH_3CHOH grouping necessary for the formation of iodoform. On the basis of these data, we concluded that 2,3-epoxypentene-4 (I), both during reaction with methanol and during rearrangement, undergoes cleavage of the oxide ring preferentially from the side of the vinyl group, due to which the main product of the reaction is 3-methoxypenten-1-ol-4 (X).

Heating of oxide (I) with 33% aqueous diethylamine to 100° gave an unsaturated aminoalcohol, apparently 3-diethylaminopenten-1-ol-4 (XI).



$$CH_3-CHOH-\underset{OCH_3}{\underset{|}{CH}}-CH=CH_2$$

(X)



$$CH_2=CH-\underset{N(C_2H_5)_2}{\underset{|}{CH}}-CHOH-CH_3$$

(XI)

EXPERIMENTAL*

The piperylene used in the work was isolated from the piperylene fraction of synthetic rubber manufactured by the process of S.V. Lebedev. Explosive peroxides of piperylene were removed beforehand by washing with 2% ferrous sulfate solution and with water, and drying over calcium chloride. The product was finally distilled in a column with an efficiency of 20 theoretical plates (b.p. 41-42°, d_4^{20} 0.6799, n_D^{20} 1.4250).

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*L.P. Redkina participated in the experimental work.

Hypochlorination of piperylene was effected in the following manner. 136 g of piperylene was shaken in a closed bottle for 3 hours with 0.8 liter of 11% solution of monochlorourea. The latter was prepared by the usual method [5]. At the conclusion of the reaction, the upper oily layer was collected, and after distilling off the unreacted piperylene it was washed many times with water for extraction of the chlorohydrins; the weight of insoluble products was 26 g. The wash liquors were combined with the aqueous layer and extracted with ether (after saturation with sodium chloride). The ethereal extract was dried with anhydrous sodium sulfate, the ether was driven off, and the reaction products distilled in vacuo. Redistillation from a flask fitted with a tall Vigreux column gave 24 g (5% on the piperylene taken) of a mixture of all of the three chlorohydrins (II), (III) and (IV).

TABLE 1

Piperylene chlorohydrins	Boiling point at 10 mm	d_4^{20}	n_D^{20}	MR_D		% Cl	
				found	calculated	found	calculated
(II)	40-41°	1.0520	1.4510	32.16	31.25	30.40	29.46
(III)	46-48	1.0594	1.4580	31.08	31.25	29.14	29.46
(IV)	80-83	1.2050	1.4731	28.05	31.25	27.22	29.46

Piperylene chlorohydrins (II), (III) and (IV) are fairly mobile, colorless liquids with a characteristic odor. They are soluble in alcohol and ether, sparingly soluble in water. Their constants are given in Table 1.

The constants of compounds (II) and (III) are in good agreement with those in the literature which referred to compounds obtained by the action of bleaching powder on piperylene [2]. The constants of compound (IV) indicate that it is not perfectly pure and contains traces of other substances.

Transformation of piperylene chlorohydrins (II) and (III) into their corresponding oxides (I) and (V) was realized by slow distillation of the chlorohydrins over 60% KOH solution taken in 4-fold excess (the chlorohydrin was introduced dropwise to the alkali heated to 100°).

From 132 g of the mixture of crude chlorohydrins (II), (III) and (IV) was obtained 38.8 g (61.5%) of a mixture of oxides (I) and (V) in the molar ratio of approximately 3 : 1. The same two substances (I) and (V) were obtained by the action of potassium hydroxide on the fractionated mixture of (II), (III) and (IV).

Piperylene oxides (I) and (V) are colorless, mobile liquids with a characteristic odor, readily soluble in alcohol and ether, insoluble in water. Judging by the refractive index, they remain substantially unchanged when stored for 2½ months.

Oxide (I): b.p. 78-81°, d_4^{20} 0.8407, n_D^{20} 1.4135, MR_D 25.01; calculated 24.26.

Found %: C 71.14; H 9.18. C_5H_8O. Calculated %: C 71.43; H 9.52.

Oxide (V): b.p. 102-104°, d_4^{20} 0.881, n_D^{20} 1.4330, MR_D 24.58; calculated 24.26.

Found %: C 71.11; H 9.39. C_5H_8O. Calculated %: C 71.43; H 9.52.

The above constants of oxides (I) and (V) are substantially identical with the constants reported in the literature [2].

Using the same method, 5 g of chlorohydrin (IV) gave about 1 g of a colorless liquid with b.p. 126-128°, d_4^{20} 0.9564, n_D^{20} 1.4275, which was not further investigated.

Isomerization of 2,3-epoxypentene-4 (I). 10 g of oxide (I) was treated with 4 g (40%) of activated alumina at 350° under the conditions previously described by us [6]. We obtained 7 g (75%) of isomerization product in the form of a mobile, colored liquid with a pungent odor. A separate sample was examined by the oxime method and found to contain 36% of carbonyl substances. At the normal pressure about 60% of the isomerization product distilled over a wide range (65-112°) in the form of a colorless liquid with a pungent odor (n_D^{20} 0.4120). Iodoform is readily precipitated when the isomerizate is treated with iodine and potassium iodide in presence of 1% NaOH. With semicarbazide in acetic acid solution it gives a semicarbazone in the form of yellowish crystals with m.p. 225°, corresponding to the semicarbazone of penten-1-one-4.

Found %: N 28.70, 29.03. $C_6H_{11}ON_3$. Calculated %: N 29.05.

Hydration of 2,3-epoxypentene-4 (I). A mixture of 8.4 g oxide and 36 ml 1% H_2SO_4 was heated in a sealed glass tube on a boiling water bath for 3 hours. The tube was then opened, the upper layer was separated, and the lower layer was saturated with potassium carbonate and extracted several times with ether. The ethereal extracts were combined with the upper layer and dried over anhydrous sodium sulfate; the ether was driven off and the reaction product was distilled in vacuo to give about 2 g of a viscous, nearly colorless liquid whose constants and analytical data corresponded to penten-4-diol-2,3 (VI).

B.p. 78-79° (10 mm) d_4^{20} 0.9931, n_D^{20} 1.4500; MR_D 27.63; calculated 27.97.

Found %: OH 32.49. $C_5H_{10}O_2$. Calculated %: OH 33.30.

Reaction of 2,3-epoxypentene-4 (I) with acetone. To a mixture (cooled to −8°) of 29 g freshly distilled acetone and 0.19 g $BF_3 \cdot O(C_2H_5)_2$ (0.5% on the total reactants) was added 8.4 g of the oxide, likewise previously cooled to −8°. After standing for 2 hours in iced water and for 12 hours at room temperature, the mixture was washed with 20 ml saturated potassium carbonate solution. After driving off the excess of acetone, the residue was distilled from a flask with a Vigreux column to give 2.4 g (17%) of 2,2,5-trimethyl-4-vinyl-dioxolane (IX) in the form of a colorless, readily mobile liquid with a pleasant odor, readily soluble in alcohol and ether, poorly soluble in water.

B.p. 128-130°, d_4^{20} 0.8927, n_D^{20} 1.4115, MR_D 39.60; calculated 39.76.

Found %: C 67.61; H 9.99. M 144.2, 143.3. $C_8H_{14}O_2$. Calculated %: C 67.51; H 9.84. M 142.4

Hydrolysis of the dioxolane (IX). 4 g of dioxolane and 5 ml 5% H_2SO_4 were shaken for 30 minutes. The acetone was then distilled off from the flask. The acetoneoxime, prepared in the usual manner, was dried over potassium carbonate (acetone with correct b.p.); it melted at 60°. The residue (after removal of the acetone) was repeatedly extracted with ether and the ethereal extract was dried over anhydrous sodium sulfate. The ether was driven off and the reaction product was fractionated in vacuo to give the above-mentioned penten-4-diol-2,3 (VI) which had been isolated on hydrolysis of (I) with 1% H_2SO_4.

B.p. 85-87° (10 mm), d_4^{20} 0.9911, n_D^{20} 1.4449, MR_D 27.45. $C_5H_{10}O_2$. Calculated 27.87.

Reaction of 2,3-epoxypentene-4 (I) with methanol. To a cooled mixture (−8°) of 19 g (6-fold excess) anhydrous methanol and 0.08 g boron fluoride etherate (0.3% of the total reactants) was added 7.5 g of the oxide, and the flask was left for 2 hours in a freezing mixture (−8°). After driving off the excess of methanol, the residue was distilled in vacuo to give 3.8 g (32.6%) of 3-methoxypenten-1-ol-4 (X).

B.p. 52-54° (15 mm), d_4^{20} 0.9241, n_D^{20} 1.4234, MR_D 32.03; calculated 32.60.

Found %: C 62.56; H 10.86; OCH_3 26.38; OH 14.41. M 113.2. $C_6H_{12}O_2$. Calculated %: C 62.15; H 10.42; OCH_3 26.72; OH 14.61. M 116.1.

The ether (X) is a colorless, readily mobile liquid with a specific odor. It is readily soluble in alcohol and ether. It forms iodoform with facility when treated with iodine and potassium iodide in presence of 10% NaOH.

Reaction of 2,3-epoxypentene-4 (I) with diethylamine. A mixture of 8.4 g oxide, 20.4 g diethylamine and 45 ml water was refluxed for 9 hours on a boiling water bath. Two layers were formed. The upper layer was collected and the lower one was saturated with KOH to separate a further small quantity of oil which was added to the main product. The latter was then dried with solid potassium hydroxide. After driving off the excess of diethylamine on a water bath at the normal pressure, the residue was fractionated in vacuo to give 4 g (21.5%) of 3-diethylaminopenten-1-ol-4 (XI) in the form of a colorless liquid (turning yellow on standing), readily soluble in alcohol and ether, insoluble in water.

B.p. 66-67° (10 mm), d_4^{20} 0.8712, n_D^{20} 1.4440, MR_D 47.90; calculated 48.76.

Found %: C 68.69; H 12.34; OH 10.96; N 9.09, 9.28. $C_9H_{19}ON$. Calculated %: C 68.80; H 12.22; OH 10.82; N 8.91.

SUMMARY

1. Reaction of piperylene with monochlorourea gave two isomeric chlorohydrins: 3-chloropenten-1-ol-4 and 1-chloropenten-3-ol-2, whose structure was confirmed by their transformation into the corresponding oxides: 2,3-epoxypentene-4 and 1,2-epoxypentene-3.

2. A study was made of the isomerization of 2,3-epoxypentene-4, its hydration, and its condensation with acetone, methanol and diethylamine.

The products of these reactions were isolated and characterized.

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**Russian translation.

PREPARATION OF PHENOLS BY CATALYTIC CONDENSATION OF ACETONE WITH ACETYLACETONE. IV.

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It was previously shown [1, 2] that condensation of acetone with alcohols (ethyl alcohol in particular) over Fe_2O_3–Al_2O_3 catalyst gives up to 10% of phenols. The proposed mechanism of their formation envisaged the dehydration of the alcohol to the corresponding aldehyde followed by condensation of the latter with acetone to form a phenol via a β-diketone or β-ketoaldehyde. In the preceding work [3] we established the formation of phenols on condensing acetone with acetaldehyde.

The objective of the present investigation was to condense acetone with a β-diketone over the same catalyst. Condensation of acetone with diketones is a neglected field of catalytic reactions. It was therefore of interest to ascertain how representatives of α-, β- and γ-diketones would behave when condensed with ketones, especially since the study of this problem has a direct bearing on the routes of formation of phenols.

We established that phenols were not formed when an equimolar mixture of diacetyl (an α-diketone) and acetone, or of acetonylacetone (a γ-diketone) and acetone, was passed over Fe_2O_3–Al_2O_3 catalyst at 400-410° at a space velocity of 31-34. Only on condensing acetylacetone (a β-diketone) with acetone was the formation of phenols observed; the main product was 3,5-dimethylphenol.

Condensations of acetylacetone with acetone were performed in the apparatus previously described [3]. The catalyst comprising 10% Fe_2O_3 and 90% Al_2O_3 was prepared from ferric nitrate and Al_2O_3 powder.

The acetylacetone employed had a boiling range of 137-139°, n_D^{20} 1.4472 and d_4^{20} 0.9734 (the literature gives n_D^{20} 1.4465, 1.4540, d_4^{20} 0.9760). The acetone boiled at 56.0-56.3° and had n_D^{20} 1.3600 (literature: n_D^{20} 1.3591).

The optimum conditions established for the reaction were similar to those found for the condensation of acetone with ethyl alcohol [2] and of acetone with acetaldehyde [3], namely: temperature of 400-410°, space velocity 31-34, equimolar ratio of reactants.

The condensates comprised two liquid layers (an oil and an aqueous layer). Phenols were extracted by two treatments of condensate with 10% NaOH followed by acidification of the alkaline solution with 10% H_2SO_4 and by extraction with ether.

The condensate obtained under the optimum conditions contained phenols (10%, or 7.4% reckoned on the mixture introduced), neutral products (31.2% or 23.2% on the mixture introduced), water (30.4%), and acetone (26.3%).

Passage of the reaction mixture over the catalyst bed was seen to be accompanied by reaction of acetylacetone with ferric oxide with formation of dark-red crystals of enol melting at 177-179° (the literature gives 179-184°). The crystals were subjected to elementary analysis.

Found %: C 50.41, 50.84; H 6.14, 6.06. $C_{15}H_{21}O_6Fe$. Calculated %: C 50.99; H 5.95.

The crystals were a product of interaction of acetylacetone with Fe_2O_3.

$$6CH_3COCH_2COCH_3 + Fe_2O_3 \longrightarrow 2Fe(C_5H_7O_2)_3 + 3H_2O.$$

This reaction caused the catalyst to lose 11% of its original weight and to give a negative reaction for iron.

The phenolic oil was fractionated. On distilling off the main fraction (217-220°) the phenol began to crystallize immediately (m.p. 62-63°); it was identified as 3,5-dimethylphenol.

Found %: OH 14.06, 14.13. M 122.3, 122.8. $C_8H_{10}O$. Calculated %: OH 13.93. M 122.0

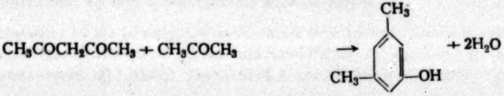
3,5-Dimethylphenoxyacetic acid (m.p. 80-81°) was prepared in good yield by the method of Holzman and Pilat [4]. A mixed melting test with 3,5-dimethylphenoxyacetic acid obtained from the phenol resulting from condensation of acetone with acetaldehyde did not show a depression. The acid was subjected to elementary analysis.

Found %: C 66.42, 66.56; H 6.78, 6.91. $C_{10}H_{12}O_3$. Calculated %: C 66.66; H 6.66.

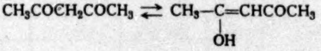
Mesityl oxide, mesitylene and phorone were identified in the neutral part of the condensate after separation in a Todd column.

Under the optimum conditions of the reaction, 1 ml of starting mixture evolved 109 ml of gas containing 47.2% CO_2, 31.9% H_2, 10.9% C_nH_{2n} and small quantities of CO and C_nH_{2n+2}.

Interaction of acetone with acetylacetone is evidently a single-stage process involving direct dehydration:



The diketone probably reacts in the enol form at the high temperature employed. It is known that even at room temperature the equilibrium between the keto and the enol form is sharply displaced in the direction of the latter.



$$CH_3COCH_2COCH_3 \rightleftarrows CH_3-\underset{\displaystyle OH}{\underset{|}{C}}=CHCOCH_3$$

Formation of 3,5-dimethylphenol as the sole phenol is evidence of the correctness of the hypothesis that formation of phenols from acetone and alcohol takes place via the intermediate step of condensation of acetone with acetylacetone. If the formation of phenols in this system had been realized by single-stage dehydration of the original molecules, then no intermediate products of formation of phenols should be found. The neutral portion of the condensate, however, contained only products of dehydration of acetone (mesityl oxide, phorone, mesitylene).

Acetylacetone was not detected in the condensate. This is due to the thermal instability of the diketone (much CO_2 was found in the exit gas). Phenols were not detected when pure acetylacetone was passed over $Fe_2O_3-Al_2O_3$ catalyst, while the CO_2 content in the gas reached 61.3%. According to the literature [5] the products of thermal breakdown of acetylacetone are acetone, acetic acid and CO_2. The thermal instability of acetylacetone also accounts for the fact that in its condensation with acetone the yield of phenols is not greater than in the system acetone-acetaldehyde.

SUMMARY

Condensation of acetone with acetylacetone over $Fe_2O_3-Al_2O_3$ catalyst gave 3,5-dimethylphenol.

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PREPARATION OF PHENOLS BY CATALYTIC CONDENSATION OF ACETONE WITH A β-KETOALCOHOL (CYCLOCONDENSATION). V.

B.N. Dolgov, L.V. Mozzhukhina and T.V. Nizovkina

Starting from the assumption that phenols can be obtained not only by catalytic condensation of acetone with a β-diketone [1, 2] but also by condensation with a β-ketoaldehyde, the objective of the present work was to study the condensation of acetone with the simplest β-ketoaldehyde over Fe_2O_3–Al_2O_3 catalyst. Bearing in mind, however, the poor thermal stability of the β-ketoaldehyde, the latter was replaced by the corresponding β-ketoalcohol. In so doing, it was assumed that over a catalyst capable of dehydrogenating ethyl alcohol to acetaldehyde, a β-ketoalcohol wouldbe transformed into β-ketoaldehyde.

The starting substances for the investigated condensation were acetone and the simplest β-ketoalcohol – butan-2-on-4-ol – which was obtained from acetone and formaldehyde [3] and had b.p. 73-75° (12 mm) and n_D^{20} 1.4302 (the literature reports n_D^{20} 1.4290). The yield of β-ketoalcohol was 60-62%.

Phenols were detected in the condensate after condensation of the ketoalcohol with acetone over Fe_2O_3–Al_2O_3 catalyst. The relation between the yield of phenols and temperature when using an equimolar ratio of reactants and a space velocity of 31-34 is shown in Table 1.

TABLE 1

Temperature	320-350°	350-360°	375-385°	400-410°	430-440°
Yield of phenols (in %)	2.1	4.0	5.7	9.6	7.5
Yield of neutral oil (in %)	9.6	14.4	25.1	37.0	22.3

The data show that the optimum temperature is 400-410°. At this temperature a study was made of the relation between yield of phenols and ratio of reactants. Results of these experiments are presented in Table 2.

TABLE 2

Molar ratio of acetone to ketoalcohol	1:3	1:1	2:1
Yield of phenols (in %)	8.3	9.5	6.8
Yield of neutral oil (in %)	23.1	36.4	25.0

These results indicate that the optimum reaction conditions at a space velocity of 31-34 are a temperature of 400-410° and an equimolar ratio of reactants. The condensate obtained under these conditions contained phenols (9.8%, or 7.3% calculated on the mixture passed through), neutral oil (37.3%, or 25.3% on the mixture passed through), unreacted acetone (24.5%) and water (24.6%). The phenols were isolated by treatment of the condensate with alkali solution, acidification of the alkali solution with 10% H_2SO_4, and extraction of the phenols with ether. The phenols, isolated in the form of an oil, were subjected to two fractional distillations. The main mass of the phenols boiled at 200-205°. A fraction was obtained with:

n_D^{20} 1.5392, d_4^{20} 1.0300, MR_D 32.97. C_7H_8O. Calculated 32.45.

A stable reddish-violet coloration, characteristic of m-cresol, was obtained with ferric chloride.

Found %: OH 15.85, 15.71. M 109.0, 108.5. C_7H_8O. Calculated %: OH 15.74. M 108.0.

An arylglycolic acid was obtained by the method of Holzmann and Pilat [4]; after recrystallization from water it melted at 101-103° in agreement with the melting point of m-cresoxyacetic acid reported in the literature (102-103°). A mixed melting test with m-cresoxyacetic acid did not give a depression. The acid was subjected to elementary analysis.

Found %: C 64.96, 64.96; H 6.13, 6.08. $C_9H_{10}O_3$. Calculated %: C 65.04; H 6.02.

A dimethylphenol was detected in the fraction boiling at 205-215°. A pure substance could not, however, be isolated; an arylglycolic acid with a very diffuse melting point was prepared. Fractional recrystallization was also unsuccessful.

Analysis of the neutral products included analysis of the fraction coming off from the condensate up to 60°, as well as of the neutral oil. The fraction coming over at up to 60° contained aldehyde (positive reaction for a silver mirror) and ketone; the latter was identified as acetone. The neutral oil was rectified in a Todd column. All of the fractions gave a positive reaction for the carbonyl group, while individual substances were identified in the 72-77° and 126-131° fractions.

The 72-77° fraction was an azeotropic mixture of methyl ethyl ketone and water (b.p. 73.6°). The constants of the ketone were determined after separation of the water.

n_D^{20} 1.3810, d_4^{20} 0.8063. The literature gives: n_D^{20} 1.3791, d_4^{20} 0.8050.

The 2,4-dinitrophenylhydrazone was prepared; after two recrystallizations from anhydrous alcohol it melted at 109-110° (literature: 111-115°). A mixture with the 2,4-dinitrophenylhydrazone of methyl ethyl ketone had the same melting point.

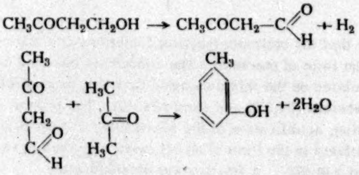
Found %: N 22.45, 22.13. $C_{10}H_{12}O_4N_4$. Calculated %: N 22.22.

The 126-131° fraction contained mesityl oxide and had n_D^{20} 1.4434 and d_4^{20} 0.8661. The fraction immediately decolorized bromine water. The 2,4-dinitrophenylhydrazone was recrystallized from anhydrous alcohol; m.p. 201-203°. A mixture with the 2,4-dinitrophenylhydrazone of mesityl oxide melted unchanged.

Found %: N 20.32, 20.23. $C_{12}H_{14}O_4N_4$. Calculated %: N 20.14.

1 ml of the starting mixture evolved, under the optimum reaction conditions, 188 ml gas containing 60.4% H_2, 25.9% CO_2 and small quantities of CO, C_nH_{2n} and C_nH_{2n+2}.

Condensation of acetone with butan-2-on-4-ol thus yielded m-cresol and neutral products (methyl ethyl ketone and mesityl oxide). The possibility of obtaining phenols from acetone and a β-ketoalcohol under conditions of heterogeneous catalysis has thus been demonstrated. m-Cresol is evidently formed in a two-step reaction:

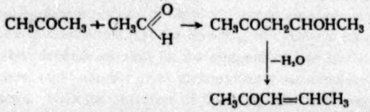


$$CH_3COCH_2CH_2OH \longrightarrow CH_3COCH_2{-}CHO + H_2$$

Formation of xylenol is associated with cleavage of the β-ketoalcohol into acetone and formaldehyde [5, 6] followed by their condensation to phenol and its higher homologs [1].

There are two possible routes to phenols from aliphatic aldehydes and ketones: 1) condensation of a mixture of aldehyde and ketone with a total of six carbon atoms and more to form an unsaturated ketone which then cyclizes to the corresponding phenol (dehydrocyclocondensation), e.g., cyclization of a mixture of acetone and n-butyraldehyde to m-cresol over chromium trioxide supported on magnesia and containing admixtures of cerium and potassium oxides [7]; 2) condensation of a mixture of aldehyde and ketone with a total number of carbon atoms less than 6 to give phenol or its homologs via intermediate formation of β-diketones and β-ketoaldehydes. In addition, V.N. Ipatyev and A.D. Petrov [8] have studied the formation of 3,5-dimethylphenol from acetone via isopborone. In this connection, however, phenols are not formed from acetone over $Fe_2O_3-Al_2O_3$ catalyst, and it is impossible on this basis to account for the formation of the other phenols that we obtained (m-cresol).

In order to clarify the possibility of formation of phenols by cyclization of unsaturated ketones, it was necessary to obtain evidence of the ability of $Fe_2O_3-Al_2O_3$ catalyst to cyclize a hydrocarbon chain containing six carbon atoms or more. Experiments with n-heptane and hepten-3-one-2 convincingly demonstrated that neither ferric oxide nor alumina possesses this ability. This conclusion is supported by the absence of isophorone from the reaction products. We can thus rule out the possibility of formation of phenols via intermediate formation of an unsaturated ketone containing only five carbon atoms:



$$CH_3COCH_3 + CH_3C{\overset{O}{\underset{H}{\lessdot}}} \longrightarrow CH_3COCH_2CHOHCH_3 \xrightarrow{-H_2O} CH_3COCH{=}CHCH_3$$

Experimental results of a study of the condensation of acetone with acetaldehyde and dicarbonyl compounds over $Fe_2O_3-Al_2O_3$ catalyst confirm the previously advanced [1] mechanism of formation of phenols:

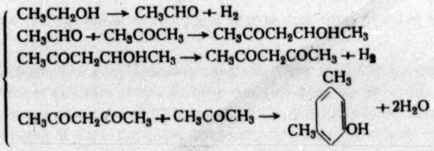
1) formation of phenols from acetone and acetaldehyde, in particular the formation of 3,5-dimethylphenol as the main product, bears witness to the participation of aldehydes in the process of formation of phenols from mixtures of alcohols and ketones;

2) in all of the condensation reactions studied, the highest yield of phenols is obtained under identical optimum conditions;

3) in all cases the phenols are formed via the steps of dehydrogenation and dehydration.

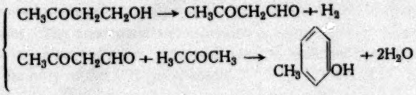
The reactions may be represented by the following equations:

I



$$CH_3CH_2OH \longrightarrow CH_3CHO + H_2$$
$$CH_3CHO + CH_3COCH_3 \longrightarrow CH_3COCH_2CHOHCH_3$$
$$CH_3COCH_2CHOHCH_3 \longrightarrow CH_3COCH_2COCH_3 + H_2$$

II



$$CH_3COCH_2CH_2OH \longrightarrow CH_3COCH_2CHO + H_2$$

4) Final confirmation of the correctness of the mechanism of formation of phenols from alcohols and ketones via intermediate formation of aldehydes, β-diketones and β-ketoaldehydes was afforded by the formation of only those phenols that enter into the above equations.

The reaction whereby phenols are formed in the systems studied can be called cyclocondensation; it constitutes a new route from aliphatic to aromatic compounds.

SUMMARY

Condensation of butan-2-on-4-ol with acetone over Fe_2O_3–Al_2O_3 catalyst gave m-cresol. A mechanism of the process, involving cyclocondensation, is proposed.

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CATALYTIC TRANSFORMATIONS OF ETHYL ACETATE UNDER PRESSURE

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In a study of the mechanism of formation of ketones from ethyl alcohol [1-3] it was established that the first step occurring over the catalyst is the dehydrogenation of ethyl alcohol to acetaldehyde, the latter then being transformed into ethyl acetate at a temperature of 225-250°. Fresh reactions take place over the catalyst at temperatures above 275° when acetaldehyde is transformed into acetone and higher ketones; intermediates in these reactions appear to be aldols. Catalytic decomposition of ethyl acetate gives products similar in composition to the products obtained from ethyl alcohol and acetaldehyde. This may be accounted for both by ketonic breakdown of the ester and by decomposition of ethyl acetate to aldehyde which then enters into a condensation reaction. It was subsequently established that the direction of catalytic transformations of primary alcohols over activated copper catalyst depends not only on the temperature but also on the pressure [4, 5]. At 350-400° and pressures above 10 atmos, ethyl alcohol gives predominantly saturated hydrocarbons with the same number of carbon atoms as the ketones. With the objective of throwing light on the mechanism of these reactions, we undertook an investigation of the catalytic breakdown of ethyl acetate over copper-thorium catalyst No. 1 [3, 6] at temperatures of 275-400° and under a hydrogen pressure of 10-100 atmos. It was established that under these conditions ethyl acetate mainly gives products similar to those obtained from ethyl alcohol under pressure, but the yield of saturated hydrocarbons under the same conditions is much smaller from ethyl acetate than from ethyl alcohol. On the basis of these observations it can be assumed that ethyl acetate is not an intermediate in the formation of ketones from ethyl alcohol.

EXPERIMENTAL

140 ml of catalyst was directly reduced with hydrogen in the reactor at atmospheric pressure and a temperature of 260-280°. The space velocity was 500 (duration of contact of about 7 seconds).

The starting substances for the reaction were ethyl acetate containing 99.2% of ester (b.p. 77.5°, n_D^{20} 1.372) and pure, dry hydrogen.

Experiments were performed in a high-pressure apparatus. With the help of a liquid pump, the ethyl acetate was injected under pressure at a rate of 120 ml/hour into an evaporator where the vapor of the ester was mixed with hydrogen introduced at a speed of 27.5 liters/hour (1 : 1 molar ratio of ester to hydrogen). The mixture entered a reactor consisting of a steel cylinder lined with copper and filled with catalyst. The reactor was heated in a hinged electric furnace containing an aluminum block. The reaction products were let down to atmospheric pressure and entered a condenser cooled to 0°. Uncondensed products passed through a trap cooled to −75° and entered a gasholder. The condensate was separated from the aqueous layer, subjected to fractional distillation, and analyzed for its content of ester, aldehyde, acid, ketones and hydrocarbons. Gaseous reaction products were analyzed with the help of the VTI gas analyzer.

In a first series of experiments with ethyl acetate, the composition of the products of reaction at 275-400° and a constant pressure of 10 atmos was investigated. The data of Table 1 and Figure 1 show that decomposition of ethyl acetate under pressure gives the same products as in the case of ethyl alcohol [4]; the yields, however, differ considerably from those with ethyl alcohol. It was established that hydrogen is not an inert medium but is consumed to a considerable extent during the reaction. At 275° there is only very slight conversion of ester into ketones; the yield of the latter is only 10%. At this temperature the greater part of the ethyl acetate is transformed into ethyl alcohol (breakdown of ester to aldehyde and hydrogenation of the latter to alcohol). About

TABLE 1

Catalytic Transformations of Ethyl Acetate in Dependence on the Temperature (pressure 10 atmos)

Temperature	Yield of condensate (in % of original ester)	Content of reaction products in condensate (in %)								Yield of gaseous products of reaction (in liters per 100 g of ester passed in)*	Composition of gaseous products of reaction (vol. %)			
		unreacted ester	acetone	methyl propyl ketone	dipropyl ketone	higher ketones (C_9)	high-boiling products (> 175°)	hydrocarbons	water		CO_2	CO	C_2H_4	C_nH_{2n+2}**
275°	75.4	31.5	6.6	3.2	0.4	0.0	0.0	0.9	0.0	26.3	46.7	17.8	1.0	34.4
300	58.5	4.8	17.3	23.2	2.0	0.0	0.0	9.5	0.0	25.3	55.6	16.9	1.8	25.6
325	60.6	1.3	18.3	25.7	7.2	2.0	5.0	8.0	0.0	11.1	63.1	33.8	traces	3.1
350	62.6	0.0	9.5	27.5	13.1	4.4	14.9	16.9	8.2	33.1	70.3	3.5	1.5	24.7
375	63.9	0.0	7.1	23.1	12.7	3.7	24.1	4.5	12.6	18.1	76.5	18.3	3.7	1.5
400	66.5	0.0	3.6	15.6	9.4	4.4	33.4	5.5	18.3	23.2	71.8	9.8	14.9	3.5

* After deducting the hydrogen added.

** Combustion index 2.6-3.8.

one-third of the original ethyl acetate generally remained unchanged. At 300-350° the content of unreacted ethyl acetate in the condensate continuously falls, and at 350° the ester is completely decomposed. At the same time the yield of ketones rises, reaching 55% at 350° (34% reckoned on the starting ester). One-half of these ketones is methyl propyl ketone. The temperature of 350° is also the optimum for formation of saturated hydrocarbons (yield 17%). Starting from ethyl alcohol, the yield of saturated hydrocarbons under the same conditions is 59% (in the condensate) [4]. A rise in temperature to 400° causes the yield of ketones and hydrocarbons from ethyl acetate to fall to 33 and 5.5% (in condensate) respectively. The amount of water and products boiling above 175° in the condensate increased considerably.

In order to determine the relation between composition of products and transformation of ethyl acetate and pressure, experiments were run at a constant temperature of 350° (optimum for the yield of ketones and hydrocarbons) and a pressure of 10 to 100 atmos. Results are presented in Table 2 and plotted in Figure 2. With increase of pressure the content of ketones in the condensate falls from 58.5% at 10 atmos to 30% at 100 atmos. This is accompanied by increased contents of water and saturated hydrocarbons in the condensate. At the same time the hydrocarbon content of the gaseous products of the reaction also increases. There is a considerable difference between the yields of products of transformation of ethyl alcohol and ethyl acetate as functions of the pressure. The products of reaction of ethyl alcohol at 80 atmos and 350° contain only 2.1% ketones and 53% saturated hydrocarbons, whereas in the case of ethyl acetate at 100 atmos and the same temperature the yield of ketones is 30.3% and that of hydrocarbons is only 21% on the weight of condensate. It can therefore be assumed that in the catalytic transformations of ethyl alcohol under pressure over activated copper catalyst the reaction goes mainly through the step of formation of acetaldehyde followed by transformation of the latter in accordance with the aldol mechanism. The conclusions previously reached in respect to ethyl alcohol [4] can be extended to ethyl acetate. The process of decomposition of the ester to aldehyde under pressure goes with a considerably lower speed than in the absence of pressure. This fact also accounts for the low yield of saturated hydrocarbons under our experimental conditions. The presence of carbon monoxide in the gas and of higher ketones and saturated hydrocarbons in the condensate indicates that the catalytic transformation of the ester goes mainly through intermediate formation of aldehyde and aldol. Acetone is possibly formed from ethyl acetate by ketonic cleavage of the ester. The presence of a large amount of CO_2

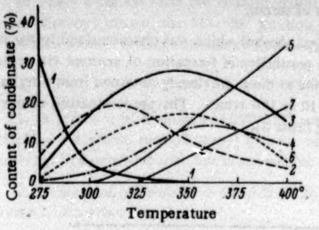

Fig. 1. Dependence of yield of products of transformation of ethyl acetate on temperature (at pressure of 10 atmos): 1) unreacted ethyl acetate; 2) acetone; 3) methyl propyl ketone; 4) dipropyl ketone; 5) high-boiling products (above 175°); 6) hydrocarbons; 7) water.

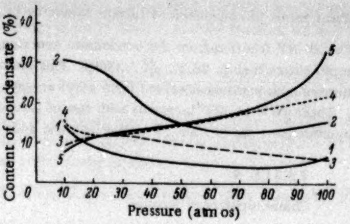

Fig. 2. Dependence of yield of products of transformation of ethyl acetate on the pressure (at 350°): 1) acetone; 2) methyl propyl ketone; 3) dipropyl ketone; 4) hydrocarbons; 5) water.

TABLE 2

Catalytic Transformations of Ethyl Acetate in Dependence on the Pressure (at 350°)

Pressure (atmos)	Yield of condensate (in % of original ester)	Content of products of reaction in condensate (in %)					Yield of gaseous products of reaction (in liters per 100 g ester passed through)*	Composition of gaseous products of reaction (in vol. %)			
		acetone	methyl propyl ketone	dipropyl ketone	hydrocarbons	water		CO_2	CO	C_2H_4	C_nH_{2n+2}**
10	57.1	14.6	30.7	9.4	15.3	7.5	19.0	62.0	15.5	0.2	22.3
20	54.3	9.0	28.9	11.6	10.7	12.7	10.0	54.8	17.1	2.6	25.5
40	75.2	6.4	17.1	10.7	14.5	12.9	20.3	70.0	2.8	3.9	23.3
60	64.2	4.5	13.5	9.6	16.2	17.4	19.3	80.8	6.9	3.0	9.3
80	66.2	3.9	13.1	7.7	19.5	21.0	14.9	70.2	5.2	1.3	23.1
100	42.4	6.2	15.6	5.6	21.0	33.0	18.8	54.9	1.7	2.7	40.7

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*Less the hydrogen introduced.

**Combustion index 2.8-3.8.

TABLE 3

Yield of Hydrocarbons in Dependence on Pressure (at 350°)

Pressure (atmos)	Content of hydrocarbons in condensate fractions (in %)				
	up to 50° (n-heptane)	50-80° (isohexane)	80-110° (n-heptane)	110-150° (C_8–C_9)	150-175° (> C_9)
10	3.6	3.5	0.4	2.9	0.8
20	1.3	2.7	0.3	2.5	0.9
40	3.0	5.1	0.8	3.3	1.0
60	4.0	3.5	1.1	5.0	1.2
80	3.9	4.2	1.1	5.8	2.0
100	6.7	2.8	4.5	3.1	1.1

in the gases points to conversion of carbon monoxide in presence of steam.

The 80-83° fraction from the condensate contained isopropyl alcohol which was characterized in the form of isopropyl chloride (b.p. 36.5°, n_D^{20} 1.3800). This indicates the possibility of formation of acetone via acetaldol. The saturated hydrocarbons obtained from ethyl acetate correspond to those previously obtained from ethyl alcohol [4]. Their yield at 350° increases with rise of pressure from 10 to 100 atmos. The predominating components of the hydrocarbons are pentane, 2-methylpentane and heptane (Table 3).

TABLE 4

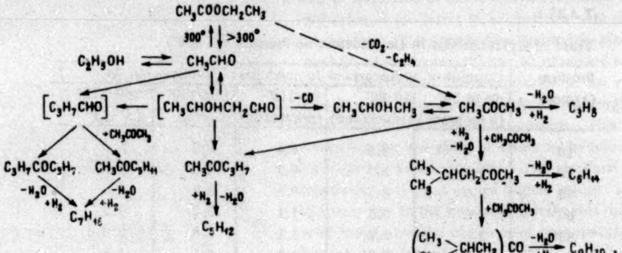
Characteristics of Ketones

Ketone	Boiling point		d_4^{20}		n_D^{20}	
	found	according to [7]	found	according to [7]	found	according to [7]
Acetone	56.0	56.0	0.7875	0.7912	1.3601	1.3591
Methyl propyl ketone	102.0	102.3	0.8057	0.8064	1.3903	1.3901
Methyl isobutyl ketone	116.6	116.8	0.8071	0.8101	1.4000	1.3959
Dipropyl ketone	144.1	144.1	0.8173	0.8175	1.4078	1.4073
Methyl n-amyl ketone	150.8	151.2	0.8187	0.8154	1.4102	1.4083
Diisobutyl ketone	168.3	168.0	0.8071	0.805	1.4128	1.412

(continuation)

Ketone	MR_D		Melting point of derivatives			
			semicarbazone		2,4-dinitrophenylhydrazone	
	found	according to [8]	found	according to [8]	found	according to [9]
Acetone	16.28	16.02	186—188	188	—	—
Methyl propyl ketone	25.36	25.28	105	105—106	139—140	143
Methyl isobutyl ketone	30.08	29.91	129	130	—	—
Dipropyl ketone	34.45	34.54	129—130	132	—	—
Methyl n-amyl ketone	34.57	34.54	120	123	—	—
Diisobutyl ketone	43.92	43.80	—	—	oil	(92)

The reactions taking place during catalytic transformation of ethyl acetate over copper activated catalyst under pressure may be represented by the following set of equations:


CH₃COOCH₂CH₃
300°
>300°
-CO₂
-C₂H₄
C₂H₅OH
CH₃CHO
[C₃H₇CHO]
[CH₃CHOHCH₂CHO]
-CO
CH₃CHOHCH₃
CH₃COCH₃
-H₂O
+H₂
C₃H₈
+CH₃COCH₃
+H₂
-H₂O
C₃H₇COC₃H₇
CH₃COC₅H₁₁
CH₃COC₃H₇
CH₃>CHCH₂COCH₃
CH₃
C₆H₁₄
C₇H₁₆
C₅H₁₂
(CH₃>CHCH₂)₂CO
CH₃
C₉H₂₀

In Table 4 are set forth the characteristics of the ketones isolated. Apart from acetone, methyl propyl ketone and dipropyl ketone, the 110-125° fraction yielded methyl isobutyl ketone, and the fraction boiling above 150° yielded methyl n-amyl ketone and diisobutyl ketone.

SUMMARY

1. In presence of hydrogen at 275-400° and a pressure of 10 atmos over activated copper catalyst, ethyl acetate gives acetone, methyl propyl ketone, methyl isobutyl ketone, dipropyl ketone and other ketones, as well as saturated hydrocarbons with the same number of carbon atoms as the ketones.

2. Increase of pressure from 10 to 100 atmos at 350° lowers the yields of ketones while raising the yield of saturated hydrocarbons and water.

3. Decomposition of ethyl acetate evidently proceeds in two directions: breakdown to two molecules of acetaldehyde and breakdown with formation of acetone.

4. Ketones are formed by aldol condensation of acetaldehyde.

5. Comparison of the experimental data on catalytic transformations of ethyl alcohol and ethyl acetate under pressure leads to the conclusion that under the conditions employed ethyl acetate is not an intermediate in the formation of ketones and saturated hydrocarbons from ethyl alcohol.

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*Original Russian pagination. See C.B. translation.

**Russian translation.

SYNTHESIS OF POLYMETHYLDIMETHYLSILOXANES

K.A. Andrianov and V.M. Mantrova

The synthesis of polyorganosiloxanes is based upon the hydrolysis and co-hydrolysis of alkyl(aryl)chlorosilanes and alkyl(aryl)alkoxysilanes in aqueous media. Hydrolysis is accompanied by formation of considerable quantities of low-molecular cyclic polymers whose transformation into high polymers is a very difficult matter. The search for other methods of transformation of organosilicon monomers into polyorganosiloxanes is a problem of definite interest. The patent literature reports that polyorganosiloxanes are obtained when alkyl(aryl)chlorosilanes are heated with alkyl(aryl)alkoxysilanes in presence of catalysts [1]. In one of our investigations [2] we studied the condensation of phenylmethyldichlorosilane with phenylmethyldiethoxysilane and showed that the reaction proceeds according to the equation

$$R_2SiCl_2 + R_2Si(OR')_2 \longrightarrow R'Cl + ClR_2Si{-}O{-}SiR_2OR' \qquad (1)$$

In the present work we investigated the condensation of methyltrichlorosilane and dimethyldichlorosilane with dimethyldiethoxysilane. In the reaction of dimethyldiethoxysilane with a mixture of methyltrichlorosilane and dimethyldichlorosilane (with a chlorine excess of 3-4%) using ferric chloride in the hydrated or anhydrous form as catalyst, ethyl chloride commenced to come off at 86-90°. The type of catalyst has a marked influence on the course of the reaction (Table 1). Although the amounts of catalyst are the same in Experiments 1-4, variations occurred in the time required for obtaining the same contents of alkoxy groups and chlorine in the polymer. The causes of the varying action of the catalyst were studied in experiments using hydrated and anhydrous ferric chloride (the weight of catalyst was 0.18% of the weight of reactants calculated on the basis of anhydrous $FeCl_3$).

TABLE 1

Expt. No.	Duration of reaction (minutes)	% content in original mixture			% content in final mixture		
		Cl	OC_2H_5	Si	Cl	OC_2H_5	Si
1	150	25.56	30.3	18.59	2.87	3.77	35.13
2	210	25.88	30.2	—	4.32	5.40	35.44
3	135	25.82	29.9	—	3.05	2.66	34.99
4	90	25.90	29.74	18.20	1.06	2.66	35.12

Notes: 1) Content of catalyst ($FeCl_3 \cdot 6H_2O$) 0.3% of weight of reactants.
2) Maximum temperature of mixture 140°.

Figure 1 contains plots of the course of condensation of dimethyldiethoxysilane with dimethyldichlorosilane and methyltrichlorosilane in presence of anhydrous and hydrated ferric chloride. The diagram shows that condensation is faster in presence of hydrated chloride than in presence of anhydrous chloride. Experiments using 0.3% of ferric chloride containing different amounts of water (Figure 2) showed that the reaction in presence of hydrated ferric chloride extends over 1½ hours, and that in presence of anhydrous chloride it extends over 9 hours; increase in the water content of the catalyst to above 40% (on the weight of $FeCl_3$) does not increase the velocity of

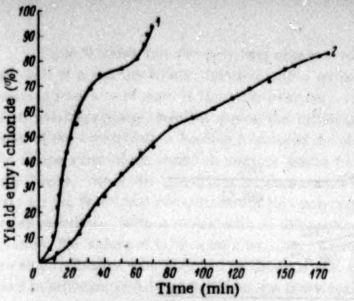


Fig. 1. Kinetics of condensation of dimethyldichlorosilane, methyltrichlorosilane and dimethyldiethoxysilane in presence of 0.18% $FeCl_3$: 1) $FeCl_3 \cdot 6H_2O$; 2) $FeCl_3$ (anhydrous).

condensation. The effect of the quantity of catalyst on the degree of condensation is plotted in Figure 3. At 140-150° in presence of 0.1% $FeCl_3 \cdot 6H_2O$, the reaction goes to the extent of 50% in 9 hours; with 0.2% $FeCl_3 \cdot 6H_2O$ it goes to the extent of 80% in 6½ hours. Experiments in which dimethyldiethoxysilane, dimethyldichlorosilane and methyltrichlorosilane were condensed at 120° in presence of various quantities of catalyst (Figure 4) also show that increase in the catalyst content from 0.1 to 0.3% influences the velocity of condensation.

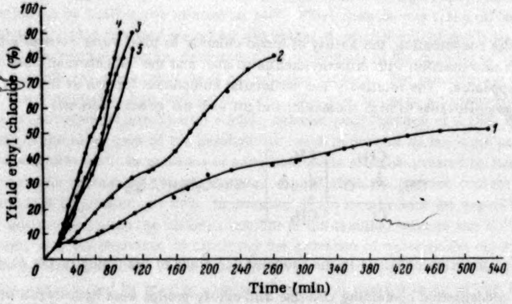


Fig. 2. Influence of content of water in ferric chloride on the velocity of condensation of dimethyldichlorosilane, methyltrichlorosilane and dimethyldiethoxysilane: 1) $FeCl_3$ (anhydrous); 2) $FeCl_3$ (anhydrous), damp; 3) $FeCl_3$ (anhydrous), 20% H_2O; 4) $FeCl_3 \cdot 6H_2O$ (40% H_2O); 5) $FeCl_3 \cdot 6H_2O$ (60% H_2O).

Examination of the experimental material shows that the heterofunctional condensation of dimethyldiethoxysilane, dimethyldichlorosilane and methyltrichlorosilane is initiated by water in the catalyst. The reaction mechanism is associated with the catalytic action of water. This is confirmed by the fact that hydrated salts like $CuSO_4 \cdot 5H_2O$ and $NiCl_2 \cdot 6H_2O$ catalyze the heterofunctional condensation while anhydrous $AlCl_3$ is substantially without catalytic action. Anhydrous ferric chloride catalyzes the reaction because, being very hygroscopic, it introduces traces of water into the reaction mixture. The most active catalyst is hexahydrated ferric chloride. In presence of hydrated ferric chloride, dimethyldichlorosilane undergoes hydrolysis with formation of dimethylchlorohydroxysilane

$$(CH_3)_2SiCl_2 \xrightarrow{FeCl_3 \cdot 6H_2O} (CH_3)_2SiCl(OH) + HCl \qquad (2)$$

The hydrogen chloride formed in this reaction reacts with dimethyldiethoxysilane

$$(CH_3)_2Si(OC_2H_5)_2 + HCl \rightarrow (CH_3)_2Si(OC_2H_5)OH + C_2H_5Cl \qquad (3)$$

The resultant hydroxy derivatives condense with loss of water:

$$(CH_3)_2SiCl(OH) + OH(OC_2H_5)Si(CH_3)_2 \xrightarrow{-H_2O} \\ \longrightarrow (CH_3)_2ClSi{-}O{-}Si(OC_2H_5)(CH_3)_2 \qquad (4)$$

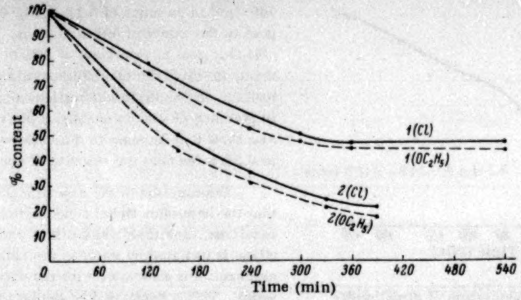
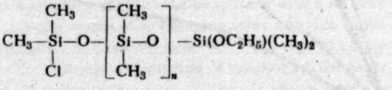


Fig. 3. Influence of concentration of ferric chloride on the velocity of condensation of dimethyldichlorosilane, methyltrichlorosilane and dimethyldiethoxysilane: 1) 0.1% $FeCl_3 \cdot 6H_2O$; 2) 0.2% $FeCl_3 \cdot 6H_2O$.

At this stage of the condensation, the ability of ferric chloride to bind water evidently becomes important. This water again enters into reaction with dimethyldichlorosilane, and the process continues until all of the functional groups have disappeared. The relatively low-molecular compounds formed at the start react with one another to give polyorganosiloxanes of high molecular weight with the general formula



$$CH_3-\underset{Cl}{\overset{CH_3}{Si}}-O-\left[\underset{CH_3}{\overset{CH_3}{Si}}-O\right]_n-Si(OC_2H_5)(CH_3)_2$$

Participation of methyltrichlorosilane in the condensation leads to branching of the chains.

The products of condensation containing chlorine and ethoxy groups were hydrolyzed with water in presence of toluene to give solutions of polydimethylsiloxane polymers. Toluene was eliminated from the polymer by prolonged standing in a thermostat at 105° until the weight was constant. In order to study the synthesized polymers more closely and to obtain data about their polydispersivity, they were fractionated by fractional precipitation. Data for individual fractions of polymers are presented in Table 2.

TABLE 2

Specimen	% yield	Molecular weight	Character of product	Elementary composition (%)			C : Si	% content of OC_2H_5
				C	H	Si		
Resin I	—	1945		31.52	8.05	36.30	2.0	1.84
1st fraction	17.75	3590	Very plastic	32.00	7.71	36.38	2.04	0.97
2nd "	15.50	2926	Viscous	30.57	7.88	37.73	1.90	0.10
3rd "	5.50	2830	Viscous	31.96	8.01	36.79	2.03	1.70
4th "	61.25	1082.6	Slightly viscous liquid	31.83	7.98	35.57	2.08	1.60
Resin II	—	7510		31.70	7.85	39.15	2.04	—
1st fraction	34.70	19890	Plastic	31.32	7.60	36.90	1.98	0.99
2nd "	9.70	8360	Viscous	32.35	7.66	36.02	2.08	—
3rd "	55.60	963	Slightly viscous liquid	32.16	8.11	36.52	2.04	3.22

Table 2 shows that the polymers obtained by heterofunctional condensation consist to the extent of over one-half of a low-molecular fraction with a molecular weight of 900-1100. The molecular weight of the remaining fractions of resin II fluctuate over very wide limits; by contrast, resin I is more homogeneous in respect of its polydispersivity, possibly due to the different conditions under which the reaction took place. The temperature of the condensation leading to resin II did not exceed 100°, the duration of the experiment was 8 hours; the temperature of the reaction mixture during formation of resin I reached 140° and the reaction duration was only 1 hour. Since the conditions for preparation of resin I are typical for a heterofunctional condensation, the data for the fractional composition of this polymer point to the homogeneity of the products of the polycondensation reactions. With a molar ratio of difunctional monomers to trifunctional monomer of 10:1 in the starting mixture, the values of C/Si should be 1.91. According to Table 2 the experimentally determined ratios of C/Si are slightly higher than required by theory. The discrepancy is due to the presence of ethoxy groups in the polymers in amounts of 0.10 to 3.22% in the individual fractions.

EXPERIMENTAL

Condensation of dimethyldiethoxysilane, dimethyldichlorosilane and methyltrichlorosilane. In a three-necked round-bottomed flask, fitted with stirrer, thermometer and reflux condenser, were placed 46 g dimethyldiethoxysilane (containing 53% of ethoxyl groups), 29.5 g dimethyldichlorosilane (containing 55.7% chlorine) and 7.5 g methyltrichlorosilane (containing 70.5% chlorine). The catalyst ($FeCl_3 \cdot 6H_2O$) was introduced (0.25 g). Condensation was effected by heating the mixture to 140°. Ethyl chloride was taken off through the condenser and a Drechsel flask (containing distilled water) for absorption of volatilized chlorosilanes. The latter were collected in a gasholder. During the reaction determinations were made of the quantity of ethyl chloride evolved and of the chlorine and ethoxyl group contents of the reaction product. The reaction was stopped when the chlorine content of the reaction product had dropped to 3-4%. The reaction gave a viscous polymer in a yield of 85-88%. Two parallel experiments (Figure 1) with a ferric chloride concentration of 0.18%, but with use in one case of anhydrous salt and in the other case of the hexahydrate, were performed by the same procedure. The experimental temperature was 120-123°. In presence of anhydrous ferric chloride (wetted by standing in the air) the reaction was carried out for 2 hours 55 minutes and was stopped when the chlorine content of the reaction mixture was 5.35%; the yield of product was 83%. In presence of the hexahydrate the experiment was carried out for 70 minutes and was stopped when the chlorine content of the reaction mixture was 6.8%; the yield of product was 85%. Experiments with the objective of clarifying the influence of water on the reaction were carried out by the same procedure. The proportion of catalyst was 0.3%. Moistening of both the anhydrous and the hexahydrated ferric chloride was effected by leaving a weighed sample of catalyst in air of high humidity. The reaction mixture comprised 43.5 g dimethyldiethoxysilane (ethoxyl group content of 56%), 29.5 g dimethyldichlorosilane (chlorine content 55.8%) and 7.5 g methyltrichlorosilane (chlorine content 70.9%). Data from these experiments are presented in Table 3.

TABLE 3

Expt. No.	Catalyst	% content of water in catalyst	Duration of reaction (minutes)	Maximum temperature of reaction mixture	% chlorine content		% yield of reaction product
					in starting mixture	in final mixture	
1	$FeCl_3$ (anhydrous)	0	530	117	27.30	15.95	94.2
2	$FeCl_3$ (anhydrous)	Humidified	273	126	27.30	5.10	93.0
3	$FeCl_3$ (anhydrous)	20	110	122	27.60	0.87	92.3
4	$FeCl_3 \cdot 6H_2O$	40	88	125	27.63	0.5	90.1
5	$FeCl_3 \cdot 6H_2O$	60	110	130	27.35	1.52	90.0

Experiment 1 was stopped when ethyl chloride substantially ceased to come off from the reaction mixture at the operating temperature. In experiment 2 the reaction product was a viscous liquid. An insoluble gel was detected in experiments 3-5 at the end of the reaction. Data for these experiments are plotted in Figure 2. Five experiments were carried out to clarify the influence of the concentration of hydrated ferric chloride. The procedure was similar to that previously described, and the molar ratio of components was the same. Two experiments with ferric chloride concentrations of 0.1 and 0.2% were carried out with heating to 140-150°. During the reaction determinations were made of the content of chlorine and ethoxyl groups in the reaction mixture. In presence of 0.1% catalyst the reaction substantially ceased after 6 hours, and further heating at 144-146° was without result. When using 0.2% of ferric chloride and heating to 140°, there was a rapid increase in viscosity of the reaction mixture. In the first experiment the yield was 89%, in the second it was 85%. Data for the reactions in these experiments are plotted in Figure 3. Three experiments using ferric chloride concentrations of 0.1, 0.2 and 0.3% were performed at 121-123°. Experimental conditions are given in Table 4. The quantities of ethyl chloride formed under these conditions are plotted in Figure 4.

TABLE 4

Content of $FeCl_3 \cdot 6H_2O$ (in % of wt. of starting substances)	Duration of reaction (minutes)	Maximum temperature of reaction mixture	% Content in starting mixture		% content in final mixture		Yield of product (%)
			Cl	OC_2H_5	Cl	OC_2H_5	
0.3	155	121	24.55	32.18	2.34	8.50	90.5
0.2	170	123	24.45	32.38	4.34	8.38	93.5
0.1	185	123	24.40	32.04	6.20	11.06	94.5

Hydrolysis of product of condensation. 30 g of condensation product dissolved in 30 g toluene was introduced with vigorous stirring into the hydrolyzer (a glass vessel with a jacket for circulation of water) which was equipped with stirrer, dropping funnel and thermometer. Temperature 18-20°. After the whole of the product had been introduced, the stirring was continued for 30 minutes. The oily layer was separated from the aqueous layer, washed with water until neutral to congo, dried with calcium chloride, and filtered. Polymers were isolated from the solution by evaporation of the toluene at a temperature not exceeding 105°. Yield of product of hydrolysis 78-80%.

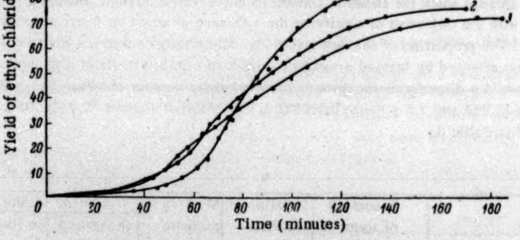


Fig. 4. Kinetics of condensation of dimethyldichlorosilane, methyltrichlorosilane and dimethyldiethoxysilane using various concentrations of ferric chloride: 1) 0.5% $FeCl_3 \cdot 6H_2O$; 2) 0.2% $FeCl_3 \cdot 6H_2O$; 3) 0.1% $FeCl_3 \cdot 6H_2O$.

Fractionation of polymers. Specimens of polymers were subjected to fractional precipitation. The work was carried out with chemically pure liquids which were dried and distilled prior to use. Benzene was used as the solvent and methanol as the precipitant. Two resins were taken for fractionation: resin I (molecular weight 1945) and resin II (molecular weight 7510). Precipitation was effected from 5% solutions in benzene at a temperature of +20°. 20 g of resin I was dissolved in 380 ml of benzene. Methyl alcohol was added dropwise from a buret with constant stirring until the liquid remained turbid. Separation of the first fraction required addition of 415 ml methanol. The solution was left for 24 hours without stirring for complete settlement of the first fraction. The mixture of solvent and precipitant was decanted off, the isolated fraction was dried at first at room temperature and later at +40° until constant in weight. The solution remaining after precipitation of the first fraction was evaporated at 40-50° to such an extent that the concentration of resin before precipitation of the next fraction was not less than on precipitation of the preceding fraction. The procedure for separation of subsequent fractions was exactly the same as for the first fraction. Precipitation of the second fraction was effected by adding 40 ml methanol, and that of the third fraction by adding 70 ml methanol. A certain proportion of the resin was not brought down even with a large excess of the alcohol; the last fraction was therefore separated by drying the residual mixture of benzene and methanol at first at room temperature and later at 40° until the residue was constant in weight. In this manner resin I gave 4 fractions. Similarly resin II yielded three fractions. A strictly constant temperature was maintained during the precipitation and separation of the fractions.

SUMMARY

1. Condensation of dimethyldichlorosilane and methyltrichlorosilane with dimethyldiethoxysilane in presence of ferric chloride led to formation of polymethyldimethylsiloxanes. Condensation took place with maximum velocity in presence of ferric chloride hexahydrate.

2. A mechanism was proposed for the condensation of dimethyldichlorosilane and methyltrichlorosilane with dimethyldiethoxysilane.

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*Original Russian pagination. See C.B. translation.

SYNTHESIS OF THIOSEMICARBAZONES AND m-IODOBENZHYDRAZONES OF SOME HALOGENATED BENZOPHENONES

E.S. Novikova and L.A. Egorshina

Thiosemicarbazones and hydrazones of various aldehydes and ketones have been synthesized in the search for active antitubercular compounds. In this connection the thiosemicarbazones and m-iodobenzhydrazones of benzophenone and its derivatives have been largely neglected. Only Feldman and Zitser [1] have published the results of tests on the tuberculostatic activity of thiosemicarbazones of benzophenone and alkoxy-, nitro-, amino- and acetamino-substituted derivatives. Very little has been published about the m-iodobenzhydrazones of benzophenone and its derivatives. Sah-Wang succeeded in preparing several hydrazones of m-iodobenzhydrazide, but the attempt to isolate the m-iodobenzhydrazone of benzophenone from the reaction mass was unsuccessful.

There is considerable evidence that the physiological activity of compounds can be enhanced by introducing a halogen into the molecule. In this connection there is also evidence that a halogen in the meta- or ortho-position intensifies the activity to a greater extent than a halogen in the para-position.

We prepared the thiosemicarbazones and m-iodobenzhydrazones of halo-substituted benzophenones (Tables 1 and 2). These compounds have not been described in the literature.

The ketones were prepared by the Friedel-Crafts reaction; their thiosemicarbazones and m-iodobenzhydrazones were obtained by condensation of the corresponding ketone with thiosemicarbazide and m-iodobenzhydrazide. The new compounds were subjected to bacteriostatic tests (results in Table 3).

The following observations can be made on the basis of the experimental data: The hydrazones of m-iodobenzhydrazide are very much less active than the thiosemicarbazones of halo derivatives of benzophenones (Table 3). A relation is found between composition and structure of the radicals entering into the composition of the thiosemicarbazones and hydrazones on the one hand and their reactivity and antibacterial activity on the other hand. In respect to reactivity towards the acid chlorides of m-iodobenzoic acid, benzene derivatives can be arranged in the order: benzene > fluorobenzene > chlorobenzene. The bacteriostatic activity of thiosemicarbazones of the corresponding ketones falls in the order: m-iodobenzophenone semicarbazone > m-iodo-p'-fluorobenzophenone thiosemicarbazone > m-iodo-p'-chlorobenzophenone thiosemicarbazone.

Accumulation of halogens in the molecule lowers the bacterial activity of a substance; for example, compounds 1 and 4 (Table 3) are more active than compounds 2 and 11. The reactivities of halo derivatives of benzophenone show a similar trend. With increasing number of halogen atoms in the molecule the chemical activity of the carbonyl group falls. For example, the yields of thiosemicarbazones and m-iodobenzhydrazones are respectively 51.3 and 19% in the case of m-iodo-p'-bromobenzophenone; they are 71 and 28% in the case of m-iodobenzophenone.

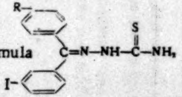
Under the conditions described below, we failed to obtain the thiosemicarbazones and m-iodobenzhydrazones of trihalo-substituted benzophenones. The position of substituents in the ring also influences the bacteriostatic and chemical activity. In the most active compounds the halogen is in the meta-position (Tables 2 and 3; compounds 6, 7, and 10, 11).

EXPERIMENTAL

The halo-substituted benzophenones, m-iodobenzhydrazide [2] and thiosemicarbazide were synthesized by

TABLE 1

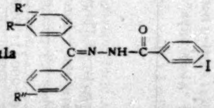
Thiosemicarbazones of the General Formula



Compound No.	R	Name of ketone	% yield	Melting point of thiosemicarbazone	Empirical formula of thiosemicarbazone	Analysis of thiosemicarbazone (%)					
						calculated			found		
						N	S	halogen	N	S	halogen
1	H	m-Iodobenzophenone	71.0	168.5—169.5°	$C_{14}H_{12}N_3IS$	11.02	8.41	33.3	11.1	8.39	33.7
2	F	m-Iodo-p'-fluorobenzophenone	61.0	201—202	$C_{14}H_{11}N_3FIS$		8.03	31.79 (iodine)	Not determined	7.9	31.24 (iodine)
3	Cl	m-Iodo-p'-chlorobenzophenone	60.0	164—165	$C_{14}H_{11}N_3ClIS$	10.11	7.71	39.06	9.76	7.68	38.8
4	Br	m-Iodo-p'-bromobenzophenone	51.3	145—146	$C_{14}H_{11}N_3BrIS$	9.13	6.95	44.95	9.05	6.81	45.0
5	CH_3	m-Iodo-p'-methylbenzophenone	55.0	181.5—182.5	$C_{15}H_{14}N_3IS$	10.63	8.11	32.11	10.96	8.10	32.02

TABLE 2

m-Iodobenzhydrazones of the General Formula



Compound No.	R	R'	R''	Name of ketone	% yield	Melting point of m-iodobenzhydrazone	Empirical formula of m-iodobenzhydrazone	Analysis of m-iodobenzhydrazone (in %)			
								calculated		found	
								N	halogens	N	halogens
6	I	H	H	m-Iodobenzophenone	33	133.5—135.5°	$C_{20}H_{14}ON_2I_2$	5.23	45.97	5.2	46.2
7	H	I	H	p-Iodobenzophenone	14	163—164	$C_{20}H_{14}ON_2I_2$	5.23	45.97	5.01	45.1
8	I	H	CH_3	m-Iodo-p'-methylbenzophenone	29	143.5—144.5	$C_{21}H_{16}ON_2I_2$	4.87	43.97	4.7	44.3
9	I	H	Br	m-Iodo-p'-bromobenzophenone	19	188—189	$C_{20}H_{13}ON_2BrI_2$	4.44	—	4.1	Not determined
10	I	H	F	m-Iodo-p'-fluorobenzophenone	7	178—179	$C_{20}H_{13}ON_2FI_2$	4.91	—	5.1	Not determined
11	H	I	F	m-Iodo-p'-fluorobenzophenone	25	164.5—165.5	$C_{20}H_{13}ON_2FI_2$	4.91	—	5.15	Not determined

the previously described methods.

Preparation of thiosemicarbazones. Into a small round-bottomed flask, fitted with a reflux condenser, were put 0.005 mole ketone, 0.005 mole thiosemicarbazide, 50 ml 98% ethanol and 3 drops of glacial acetic acid. The flask was heated on a boiling water bath for 6 hours. The mixture was then cooled, and the precipitate was filtered, washed with a little ethanol and recrystallized from alcohol until the melting point was unchanged. Nitrogen was determined by the Kjeldahl method and chlorine by the Carius method. The results of the syntheses are given in Table 1.

Preparation of m-iodobenzhydrazones. A mixture of equimolar quantities of ketone and m-iodobenzhydrazide (0.00125 mole of each), 3-5 drops of glacial acetic acid and 30-40 ml 98% ethanol was refluxed in a flask on a boiling water bath for $4\frac{1}{2}$ hours. After cooling, the precipitate was filtered and purified by recrystallization from ethanol. The products were then quantitatively analyzed for nitrogen (Kjeldahl) and chlorine (Carius). Results are given in Table 2.

The microbiological investigation was carried out by the surface film method on a liquid potato medium with a strain of tubercular bacteria of the "Akademiya" type. Samples were kept in a thermostat for 8-10 days. Results of tests are presented in Table 3.

TABLE 3

Bacteriostatic Activity of Thiosemicarbazones and m-Iodobenzhydrazones Towards the Tubercular Strain "Akademiya"

Number of compound	Dilution			
	1:100,000	1:200,000	1:400,000	1:800,000
1		−	−	+
2		−	+	++
3	−	−	++	
6	−	+	++	
7	+	+	+++	
10	−	++	+++	
11	−	++	++	
Control	+++	+++	+++	

Note: Minus (−) denotes absence of growth of film, plus (+) denotes insignificant growth of film in comparison with control, two pluses (++) denote slowing-down of growth of film in comparison with control, three pluses (+++) signify that growth of film corresponds to the control.

SUMMARY

Thiosemicarbazones and m-iodobenzhydrazones of some halo derivatives of benzophenone were synthesized. These compounds had not hitherto been described in the literature. A relation was noted between chemical activity of the carbonyl group in the substituted benzophenones and the composition, structure and bacteriostatic activity of the prepared compounds.

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*Original Russian pagination. See C.B. translation.

DIALKYLAMIDES OF TRICHLOROPHOSPHAZOSULFURIC ACID AND CHLORIDES OF N,N-DIALKYLSULFAMIDO-N'-PHOSPHORIC ACID

A.V. Kirsanov and Z.D. Nekrasova

Of the derivatives of trichlorophosphazosulfuric acid, only its chloride [1] and the bis(trichlorophosphazo)-sulfone [2] are known up to now.

The dimethyl- and diethylamides of trichlorophosphazosulfuric acid are described in this paper; these were obtained by the reaction of phosphorus pentachloride with N,N-dimethyl- and N,N-diethylsulfamide by the scheme

$$(CH_3)_2NSO_2NH_2 + PCl_5 \longrightarrow 2HCl + (CH_3)_2NSO_2N{=}PCl_3.$$

The reaction proceeds under mild conditions in almost quantitative yields. The dimethylamide of trichlorophosphazosulfuric acid is a low-melting crystalline substance, while the diethylamide is a liquid. The dialkylamides of trichlorophosphazosulfuric acid react easily with water, alcohols, phenols, amines and other compounds containing active hydrogen atoms, as do all other trichlorophosphazo sulfones [3]. The dialkylamides of trichlorophosphazosulfuric acid are more stable to heat than the chloride of trichlorophosphazosulfuric acid [4], and can be distilled in a high vacuum without decomposition. The structure of the dialkylamides of trichlorophosphazosulfuric acid is shown by their quite rigid method of preparation, the nearly quantitative yields by the above indicated scheme, the analytical data, and their chemical properties.

When treated with water, or, even better, with formic acid [5], the dialkylamides of trichlorophosphazosulfuric acid can be transformed in turn into all of their possible phosphorus-containing hydrolysis products, i.e., the N,N-dialkylsulfamido-N'-phosphoric acid dichlorides, the N,N-dialkylsulfamido-N'-phosphoric acid monochlorides and the free N,N-dialkylsulfamido-N'-phosphoric acids, in accord with the scheme

$$(CH_3)_2NSO_2N{=}PCl_3 \xrightarrow{+HCOOH} (CH_3)_2NSO_2NHPOCl_2 \xrightarrow{+HCOOH}$$
$$\longrightarrow (CH_3)_2NSO_2NHPO(OH)Cl \xrightarrow{+HCOOH} (CH_3)_2NSO_2NHPO(OH)_2.$$

The first step of the hydrolysis proceeds easily at room temperature, while the second and third steps proceed with considerably greater difficulty (only with long heating).

EXPERIMENTAL

Dimethylamide of trichlorophosphazosulfuric acid. A mixture of 30 ml of carbon tetrachloride, 0.04 mole of N,N-dimethylsulfamide and 0.04 mole of phosphorus pentachloride was heated under reflux on a bath (85-100°). To control the reaction the upper end of the condenser was connected to a gas bubbler, filled with sulfuric acid. The evolved hydrogen chloride was trapped in water. The reaction is completely ended in 1 hour, and here 98.5% of the theoretical amount of hydrogen chloride is evolved. The hot solution was filtered. On cooling the dimethylamide of trichlorophosphazosulfuric acid deposits as coarse, colorless, transparent, rectangular plates. The product was vacuum-filtered, washed with cold carbon tetrachloride, and vacuum-dried. All of the operations should be run in such manner that both the solutions and substance are exposed as little as possible to atmospheric moisture. Yield 99.0%, m.p. 73-75°. The reaction can also be run without solvent. The dimethylamide of trichlorophosphazosulfuric acid reacts slowly with water and vigorously with alcohol, is readily soluble in benzene, dichloroethane and ethyl acetate, and is difficultly soluble in cold carbon tetrachloride and petroleum ether.

Found %: Cl 40.9, 41.01; equiv. after hydrolysis 4.96, 4.98. $C_2H_6O_2N_2SCl_3P$. Calculated %: Cl 41.03; equiv. after hydrolysis 5.00.

Diethylamide of trichlorophosphazosulfuric acid. A mixture of 0.05 mole of N,N-diethylsulfamide and 0.05 mole of phosphorus pentachloride was heated on the bath at 80°. The reaction was complete in 20 minutes. To completely remove the hydrogen chloride the reaction product was heated in vacuo for 10 minutes at 80°. The residue was essentially the diethylamide of trichlorophosphazosulfuric acid as a nearly colorless, transparent liquid. The yield was theoretical. When pure starting compounds are used the reaction product does not require further purification. The diethylamide of trichlorophosphazosulfuric acid reacts vigorously with water and with alcohol, is readily soluble in benzene, carbon tetrachloride, dichloroethane, chloroform and acetone, and is difficultly soluble in ether and petroleum ether; d_4^{20} 1.4665, n_D^{20} 1.5072.

Found %: Cl 37.10, 37.12. Equiv. after hydrolysis 4.85, 5.03. $C_4H_{10}O_2N_2SCl_3P$. Calculated %: Cl 37.04. Equiv. after hydrolysis 5.00.

The previously unknown N,N-diethylsulfamide was obtained by treating the chloride of diethylsulfamic acid with ammonia. N,N-Diethylsulfamide is a colorless substance, crystallizing from carbon tetrachloride as large plates; m.p. 46-47°; readily soluble in water, alcohol and acetone, more difficultly soluble in ether and benzene, and slightly soluble in either boiling carbon tetrachloride or petroleum ether.

Found %: N 18.52. $C_4H_{12}O_2N_2S$. Calculated %: N 18.43.

Dichloride of N,N-dimethylsulfamido-N'-phosphoric acid. To a solution of 0.01 mole of the dimethylamide of trichlorophosphazosulfuric acid in 10 ml of benzene was added 0.01 mole of anhydrous formic acid. The reaction began immediately, accompanied by the slight warming of the mixture and the evolution of hydrogen chloride and carbon monoxide. Soon the crystalline dichloride began to separate. After 12 hours the product was vacuum-filtered and recrystallized from carbon tetrachloride. Yield 93.0%; m.p. 110-112°; yield of hydrogen chloride 94.0%.

The dichloride of N,N-dimethylsulfamido-N'-phosphoric acid reacts with water much slower than does the dimethylamide of trichlorophosphazosulfuric acid. It crystallizes from carbon tetrachloride as thin, colorless needles, readily soluble in ethyl acetate and acetone. On heating it dissolves in benzene, dichloroethane and chloroform, is more difficultly soluble in carbon tetrachloride and petroleum ether, and is insoluble in ether.

Found %: Cl 29.60, 29.36. Equiv. after hydrolysis 4.00, 3.99. $C_2H_7O_3N_2SCl_2P$. Calculated %: Cl 29.40. Equiv. after hydrolysis 4.00.

Dichloride of N,N-diethylsulfamido-N'-phosphoric acid. The synthesis was run in the same manner as for the dimethyl derivative, but here the reaction product does not precipitate from solution, being fairly soluble in benzene. After standing for 12 hours the benzene was vacuum-distilled at 30-35°; the residue was a light-yellow oil, which crystallized completely when rubbed with a glass rod. The yield was theoretical; after recrystallization from carbon tetrachloride, m.p. 70-72°. The dichloride of N,N-diethylsulfamido-N'-phosphoric acid is readily soluble in chloroform, acetone and dichloroethane, soluble when heated in carbon tetrachloride or ether, and difficultly soluble in hot petroleum ether. It crystallizes from petroleum as spherical agglomerates of fine needles.

Found %: Cl 26.41, 26.45. Equiv. after hydrolysis 4.01, 4.05. $C_4H_{11}O_3N_2SCl_2P$. Calculated %: Cl 26.39. Equiv. after hydrolysis 4.00.

Monochloride of N,N-Dimethylsulfamido-N'-phosphoric acid. A mixture of 0.01 mole of the dichloride of N,N-dimethylsulfamido-N'-phosphoric acid, 0.01 mole of anhydrous formic acid and 50 ml of benzene was boiled under reflux for 5 hours. Almost the theoretical amount of hydrogen chloride was evolved in this time. A crystalline precipitate deposited on cooling, which was vacuum-filtered, washed with benzene, and vacuum-dried. Yield 60.0%; m.p. 74-80° (with decomposition).

The monochloride of N,N-dimethylsulfamido-N'-phosphoric acid is soluble in chloroform, acetone, dichloroethane and hot dioxane, very difficultly soluble in boiling carbon tetrachloride, and insoluble in benzene.

Found %: Cl 16.01, 16.12. Equiv. after hydrolysis 3.06, 3.07. $C_2H_8O_4N_2SClP$. Calculated %: Cl 15.95. Equiv. after hydrolysis 3.00.

Monochloride of N,N-diethylsulfamido-N'-phosphoric acid. A mixture of 0.01 g of the dichloride of N,N-diethylsulfamido-N'-phosphoric acid, 100 ml of benzene and 0.01 mole of anhydrous formic acid was boiled under reflux for 5 hours. The solution after cooling was decanted from the oily viscous mass (free N,N-diethylsulfamido-N'-phosphoric acid) and the solvent was evaporated in vacuo. The residue, a colorless viscous oil, was the monochloride of N,N-diethylsulfamido-N'-phosphoric acid. Yield 66.2%. For purification the substance was precipitated from benzene solution with petroleum ether and any residual solvent was removed by heating at 50° in vacuo.

Found %: Cl 14.06. Equiv. after hydrolysis 2.93. $C_4H_{12}O_4N_2SPCl$. Calculated %: Cl 14.17. Equiv. after hydrolysis 3.00.

The monochloride is readily soluble in acetone, chloroform and ethyl acetate, more difficultly soluble in benzene (about 4%), and insoluble in carbon tetrachloride, dichloroethane, ether and petroleum ether.

N,N-dimethylsulfamido-N'-phosphoric acid. A mixture of 0.01 mole of the dichloride of N,N-dimethylsulfamido-N'-phosphoric acid, 0.02 mole of anhydrous formic acid and 50 ml of dioxane was boiled under reflux for 10 hours. Gradually a glassy, hard, crystalline mass deposited on the sides of the flask, which was suction-filtered, washed with dioxane, and vacuum-dried. Yield 92.1%; m.p. 187-189° (decomposition). N,N-Dimethylsulfamido-N'-phosphoric acid is soluble in water, and insoluble in benzene, acetone, carbon tetrachloride, dioxane, ether and petroleum ether.

Found equiv. 1.91, 2.05 (phenolphthalein). $C_2H_9O_5N_2SP$. Calculated equiv. 2.00.

N,N-Diethylsulfamido-N'-phosphoric acid. A mixture of 0.01 mole of the monochloride of N,N-diethylsulfamido-N'-phosphoric acid, 100 ml of benzene and 0.01 mole of anhydrous formic acid was boiled under reflux until the evolution of hydrogen chloride ceased. As the N,N-diethylsulfamido-N'-phosphoric acid was formed it deposited from solution as a viscous oil, which gradually crystallized. The reaction required about 10 hours for completion. The benzene was decanted, the precipitate washed well with dioxane, rapidly pressed on a porous plate, and then dried in vacuo. N,N-Diethylsulfamido-N'-phosphoric acid was obtained as fine crystals of indefinite shape, rapidly deliquescing in the air; the compound is readily soluble in water and alcohol, very difficultly soluble in dioxane, and insoluble in benzene, ether and carbon tetrachloride. Yield 81.0%; melting point not sharp (start about 80°, end about 95°).

Found: equiv. 1.99 (phenolphthalein), 1.04 (methyl orange). Calculated: equiv. 2.00 (phenolphthalein), 1.00 (methyl orange).

SUMMARY

The N,N-dimethyl- and N,N-diethylamides of trichlorophosphazosulfuric acid were prepared, as well as all of their theoretically possible phosphorus-containing hydrolysis products.

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THE MECHANISM OF THE GAS-PHASE CATALYTIC REACTION OF ACETYLENE AND ACETIC ACID

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The main products of the gas-phase catalytic fraction of acetylene and acetic acid are vinyl acetate (v.a.) and ethylidene diacetate (e.d.a.). According to the literature [1-4], the optimum conditions for the preparation of vinyl acetate are: molar ratio $C_2H_2 : CH_3COOH = 10\text{-}25 : 1$, 180-220°, space velocity – 150-250 liters/liter of catalyst per hour, and catalyst – zinc acetate on a carrier.

The yield of ethylidene diacetate increases, and the yield of vinyl acetate decreases in measure with decrease in the amount of excess acetylene.

In the opinion of investigators, ethylidene diacetate is formed as the result of subsequent addition of acetic acid to the vinyl acetate. Consequently, the role of excess acetylene in the synthesis of vinyl acetate reduces to its displacing the formed vinyl acetate from the surface of the contact catalyst and in that way preventing its further reaction with acetic acid. The postulations indicated above were made without any experimental confirmation and, in particular, without a study of the kinetics of the separate stages of the process. In addition, none of the investigators took into consideration the fact that acetic acid in the vapor phase exists not only as the monomer, but also as the dimer.

According to the most reliable experimental data [5], the equilibrium of the reaction $(CH_3COOH)_{2(g)} \rightleftharpoons 2CH_3COOH_{(g)}$ is expressed by the equation

$$\log K_p = -\frac{3200}{T} - 7.715 + 0.03 \qquad (1)$$

With increase in the temperature the equilibrium is shifted to the right, and practically complete dissociation of the acetic acid dimer occurs at quite high temperatures (~300°). It can be achieved at lower temperatures only by evacuation (or dilution). Under the conditions of running the synthesis (180-220°) this makes it necessary to consider the reaction of acetylene and vinyl acetate with both the monomer and dimer of acetic acid.

Thermodynamics of the reaction of acetylene and vinyl acetate with acetic acid. Below, in Table 1, are given the principal thermodynamic parameters of the reaction components, in part taken from the most reliable sources (acetylene, acetic acid) [6, 7] or calculated by us using the method of Hougen and Watson [6] (vinyl acetate, ethylidene diacetate).

The following equilibria were calculated: a) the formation of vinyl acetate in the reaction of acetylene with the monomer and dimer of acetic acid

$$C_2H_2 + CH_3COOH_{(g)} \rightleftharpoons CH_2{=}CHOCOCH_{3(g)}$$

$$\log K_{p_1} = \frac{4530}{T} - 3.02\log T + 1.27 \cdot 10^{-3}T + 1.64 \qquad (2)$$

$$C_2H_2 + \frac{1}{2}(CH_3COOH)_{2(g)} \rightleftharpoons CH_2 = CHOCOCH_{3(g)}$$

$$\log K_{p_2} = \frac{2810}{T} - 3.0\log T + 0.6 \cdot 10^{-3}T + 6.14 \qquad (3)$$

b) The formation of ethylidene diacetate in the reaction of acetylene with the monomer and dimer of acetic acid

$$C_2H_2 + 2CH_3COOH_{(g)} \rightleftarrows CH_3CH(OCOCH_3)_{2\,(g)}$$

$$\log K_{p_3} = \frac{6570}{T} - 3.9 \log T + 2.3 \cdot 10^{-3} T - 4.55 \tag{4}$$

$$C_2H_2 + (CH_3COOH)_{2\,(g)} \rightleftarrows CH_3CH(OCOCH_3)_{2\,(g)}$$

$$\log K_{p_4} = \frac{3040}{T} - 3.87 \log T + 0.98 \cdot 10^{-3} T + 4.5 \tag{5}$$

$$CH_2{=}CHOCOCH_{3\,(g)} + CH_3COOH_{(g)} \rightleftarrows CH_3CH(OCOCH_3)_{2\,(g)}$$

$$\log K_{p_5} = \frac{1870}{T} - 0.98 \log T + 1.04 \cdot 10^{-3} T - 6.1 \tag{6}$$

$$CH_2{=}CHOCOCH_{3\,(g)} + \frac{1}{2}(CH_3COOH)_{2\,(g)} \rightleftarrows CH_3CH(OCOCH_3)_{2\,(g)}$$

$$\log K_{p_6} = \frac{240}{T} - 0.8 \log T + 0.39 T - 1.1 \tag{7}$$

From the data presented in Table 2 it follows that: a) the formation of vinyl acetate is possible in the reaction of acetylene with either the monomer or dimer of acetic acid in a wide temperature interval; the value of a clear up to 300° is close to unity, and b) the formation of ethylidene diacetate in the reaction of acetylene with acetic acid is possible only as the result of the simultaneous addition of two molecules of the monomer to acetylene at 180-200° (which is less probable, since here a triple collision is required) or of one molecule of the acetic acid dimer (up to 300-320°). In general, the formation of e.d.a. is impossible in the reaction of vinyl acetate with acetic acid in the gas phase.

TABLE 1

Compound	ΔH°_{298} (kcal)	S°_{298}	a	$b \cdot 10^3$	$C \cdot 10^6$
Acetylene C_2H_2	54.19	47.997	5.84	15.28	− 5.52
Acetic acid (monomer) CH_3COOH	−104.58	67.52	4.0	46.2	−16.35
Acetic acid (dimer) $(CH_3COOH)_2(g)$*	−224.26	96.44	7.92	104.7	−46.8
Vinyl acetate $CH_2{=}CHOCOCH_3(g)$	− 72.3	86.4	3.83	73.13	−25.29
Ethylidene diacetate $CH_3CH(OCOCH_3)_2(g)$	−185.85	115.6	6.02	128.99	−55.35

*The gaseous phase is indicated in this manner here and below.

Since the thermodynamic parameters for vinyl acetate and ethylidene diacetate, calculated by us using the Hougen method [6], cannot pretend to be absolutely accurate, then also the calculations of the equilibria of the possible reactions are, naturally, approximate and require experimental verification.

EXPERIMENTAL

A. Method of operation. The experiments were run in a flow system. The vapor-gas mixture, composed of purified acetylene [8] and acetic acid (c.p., m.p. −16.7°), entered the contact tube, where it was first heated to the reaction temperature by passage through a layer of glass packing, placed ahead of the catalyst. The exact feeding of the acid, added from a vaporizer, was accomplished by means of a relay and heat regulator, while a rheometer was used for feeding the acetylene. The contact tube was contained in an electric furnace with automatic temperature control (accuracy ± 1°). The reaction products passed in sequence through a condenser with

TABLE 2

T (°K)	K_{p_1}	α_1	K_{p_2}	α_2	K_{p_3}	α_3	K_{p_4}	α_4	K_{p_5}	α_5	K_{p_6}	α_6
450	$1.6 \cdot 10^4$	0.993	$5 \cdot 10^4$	0.995	6.0	0.56	28.8	0.81	$8.3 \cdot 10^{-5}$	~ 0	$3.1 \cdot 10^{-3}$	0.003
500	$1.5 \cdot 10^3$	0.98	$9.1 \cdot 10^3$	0.992	$2.2 \cdot 10^{-1}$	0.07	4.5	0.57	$3.3 \cdot 10^{-5}$	~ 0	$2.6 \cdot 10^{-3}$	0.003
550	2.10	0.93	$2.3 \cdot 10^3$	0.99	$8 \cdot 10^{-3}$	~ 0	$9.1 \cdot 10^{-1}$	0.28	$1.6 \cdot 10^{-5}$	~ 0	$2.4 \cdot 10^{-3}$	0.003
600	34.6	0.83	$6.7 \cdot 10^2$	0.98	$6.8 \cdot 10^{-4}$	~ 0	$2.6 \cdot 10^{-1}$	0.1	$8.1 \cdot 10^{-6}$	~ 0	$2 \cdot 10^{-3}$	0.003

receiver, where the main portion of the liquid products condensed, and then through a trap, immersed in a Dewar vessel and cooled with a mixture of dry ice and methanol, where the vinyl acetate, failing to condense in the receiver, was trapped. The readings in all cases were begun 1.5-2 hours after the start of passing the mixture, when a stationary condition had been established. The activity of the catalyst was checked by the reproducibility of the experimental results. The vinyl acetate used in a number of experiments had the following constants: b.p. 72.0-72.5° (754 mm), d_4^{20} 0.9340. The nitrogen was purified from oxygen impurities by passage through hydrosulfite solution and then over copper, deposited on silica gel, at 360-380°.

B. Method of analysis. The acetic acid was determined by titration with 0.1N NaOH, the vinyl acetate by bromination [1], and the ethylidene diacetate by saponification, using 0.5N NaOH and boiling for 2 hours. The analysis data were checked by distillation of the condensate.

C. Catalysts. Specimen No. [illegible] was prepared by the impregnation of previously degasified AR-3 charcoal with zinc acetate solution. The zinc acetate content was 25%. Specimen No. 2 was zinc acetate, deposited on activated γ-Al_2O_3. The zinc acetate content was $\sim$30%. This catalyst was used at the higher temperatures (270-290°).

Experimental Data and Discussion of Results

Influence of the $C_2H_2 : CH_3COOH$ ratio on the character of the products formed. The experiments were run at 200° in the presence of catalyst No. 1. In some cases the acetylene was diluted with nitrogen. The time of the experiments was 1-1.5 hours. The total space velocity was 250-270 liters/liter catalyst/hour. The results of some of the experiments are summarized in Table 3.

From the obtained results it can be seen that the ratio of the formed vinyl acetate and ethylidene diacetate depends only on the partial content of acetic acid in the starting mixture, independent of whether this is achieved by dilution with acetylene or with a mixture of acetylene and nitrogen. The lower the partial content of acetic acid, the higher the yield of vinyl acetate and the lower the yield of ethylidene diacetate, and the reverse. Consequently, the role of excess acetylene reduces only to a decrease in the partial content of acetic acid, which favors an increase in the degree of dissociation of the dimer with the formation of the monomer. Here the probability of acetylene reacting with the acetic acid monomer increases, which leads to the formation of vinyl acetate.

Influence of the space velocity on the nature of the products formed. The experiments were run with the molar ratio $C_2H_2 : CH_3COOH = 1 : 1$ in the presence of catalyst No. 2. The first four experiments were run at 270°, while the last were run at 290°. From the data in Table 4 it can be seen that at both 270 and 290° the yield of ethylidene diacetate increases with increase in the space velocity. The only explanation for these facts is that at substantial values for the space velocity the acetic acid dimer fails to dissociate completely, and its concentration proves to be above the equilibrium concentration. This leads to an increase in the probability of acetylene reacting with the dimer of acetic acid, as a result of which ethylidene diacetate is formed. If the formation of ethylidene diacetate represented a consecutive reaction, as is believed by a number of investigators [1-4], then the reverse picture should obtain, i.e., the yield of e.d.a. should have increased with decrease in the space velocity (with increase in the contact time).

In addition, by means of special experiments it was established by us that in not a single case is ethylidene diacetate formed when an equimolar mixture of vinyl acetate and acetic acid is passed through the tube at 220, 240 and 290°.

TABLE 3

$C_2H_2 : N_2 : CH_3COOH$	Degree of acetic acid conversion (in %)	Percent acetic acid, consumed for the formation of		Yield based on reacted acid (in %)	
		v.a.	e.d.a.	v.a.	e.d.a.
16:0:1	87.3	84	0.0	96.2	–
10:0:1	87.6	82.5	2.1	94.1	2.4
1:9:1	86.8	82.3	2.3	94.8	2.6
1:9:1	87.4	82.7	2.5	94.5	2.8
6.5:0:1	68.3	60.6	4.4	88.8	6.5
4:0:1	42.4	33.8	7.2	79.7	17.0
1:3:1	43.3	33.0	7.8	76.2	18.0
2:0:1	29.6	20.2	8.4	68.3	28.4
1:0:1	19.4	10.2	8.3	52.6	42.7

TABLE 4

Total space velocity (in liters/liter catalyst/hour)	Degree of acetic acid conversion (in %)	Yield based on reacted acid (in %)	
		v.a.	e.d.a.
250	49	92.0	0.0
400	40.4	84.0	9.4
500	38.2	82.0	10.6
600	27.4	78.0	12.4
300	43.5	98.0	0.0
600	32.4	90.5	4.5
1200	26.3	86.2	9.8

Substantial decomposition of the vinyl acetate is observed at 290°.

As a result, the experimental data obtained by us, supporting the results of the thermodynamic analysis of the process, permit making the following conclusions. 1) In the gas-phase catalytic process both vinyl acetate and ethylidene diacetate are formed directly in the reaction of acetylene with acetic acid. The reaction of acetylene with the monomer of acetic acid leads to the formation of vinyl acetate, and with the dimer – to ethylidene diacetate. 2) The two reactions are parallel and are determined by the content of the monomeric and dimeric forms of acetic acid in the reaction mixture

$$C_2H_2 + CH_3COOH_{(r)} \rightleftarrows CH_2{=}CHOCOCH_{3(r)}$$

$$C_2H_2 + (CH_3COOH)_{2\,(r)} \rightleftarrows CH_3CH(OCOCOO_3)_{2\,(r)}$$

The simultaneous adsorption of acetylene together with the monomer and dimer of acetic acid leads to the formation of two types of adsorption complexes: a) in the adsorption of the dimer – $C_2H_2 \cdot Zn(CH_3COO)_2 \cdot \cdot (CH_3COOH)_2$, and b) in the adsorption of the monomer – $C_2H_2 \cdot Zn(CH_3COO)_2 \cdot CH_3COOH$. Suitable redistribution of the bonds should yield: in the first case – ethylidene diacetate, and in the second – vinyl acetate. As a result, the character of the final reaction products will be determined by the nature of the intermediate adsorption complexes formed.

SUMMARY

On the basis of thermodynamic analysis some theories were expressed, supported by experimental study, regarding the mechanism for the formation of vinyl acetate and ethylidene diacetate in the reaction of acetylene with acetic acid.

It was established that ethylidene diacetate is formed in the direct reaction of acetylene with the dimer of acetic acid, while vinyl acetate is formed in the reaction of acetylene with the monomer of acetic acid on the surface of the catalyst.

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CATALYTIC REARRANGEMENTS OF SOME ACETYLATED ARYLAMINES

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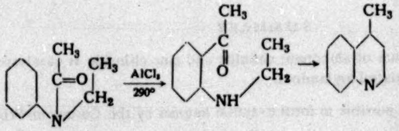
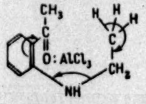
The possibility of forming aminoacetophenones in the thermal rearrangement of acetanilide was established by Meyer and Hofmann [1]. D.N. Kursanov [2], using aluminum chloride for the rearrangement, comparable to the Fries reaction [3] for phenol ethers, obtained some p-amino ketones in 5-10% yield. A mechanism was postulated for the rearrangements consisting in the intermediate formation of acetyl chloride and subsequent progress of the reaction comparable to the Gustavson-Friedel-Crafts method for the synthesis of ketones, which received experimental confirmation [4]. Since cases of the direct introduction of an acetyl radical in the ortho position to the amino group are not described in the literature, the postulation was expressed that only p-amino ketones are formed in the rearrangements of acetylated arylamines [2].

The catalysts investigated by us for the rearrangements were $AlCl_3$, $ZnCl_2$, $SnCl_4$, P_2O_5, $AlCl_3 + ZnCl_2$. $ZnCl_2$ or the mixed catalyst gave the best results, and here it was possible to obtain by rearrangement the o-amino ketones or their subsequent condensation products. Thus, the gradual addition of acetanilide to $ZnCl_2$ at a temperature not exceeding 160° gave, together with p-aminoacetophenone, also flavaniline, the condensation product of p- and o-aminoacetophenone [5], while in the case of aceto-p-toluidide the use of the mixed catalyst gave 2-amino-5-methylacetophenone.

The possibility of the direct nuclear acetylation of arylamines in the ortho position to the amino group was also established by us, which is not achieved by earlier described methods [6, 7]. Migration of the acetyl radical ortho to the amino group was observed in the rearrangement of N-ethylacetanilide with either $AlCl_3$ or the mixed catalyst. The use of $ZnCl_2$ for the rearrangement was described by Pictet and Bunzl [8], who established that the ethyl radical shifts, which after cyclization leads to the formation of quinaldine. Earlier it was shown [9] that the formation of quinaldine goes through the α,β-dimethylindole state, and this excludes the formation of lepidine by the Pictet reaction using $ZnCl_2$. In our case of using $AlCl_3$ as the catalyst the ethylacetanilide rearranges into lepidine in accord with the scheme



In this case a shift of the acetyl radical can be explained on the basis of a weakening of the bond between the acetyl group and the nitrogen due to its polarization at the carbonyl group in the formation of a stable complex with the aluminum chloride (in contrast to $ZnCl_2$), and the cyclization as proceeding, not at the methylene group (which leads to the formation of quinaldine), but at the methyl group, which leads, as the result of σσ-conjugation [10] in the side chain of o-ethylaminoacetophenone, to the formation of lepidine.



The mechanism for the rearrangements of acetanilides using $ZnCl_2$ is also different from the mechanism using $AlCl_3$, and is apparently the result of an intramolecular shift of the acetyl radical; here the first stage is the formation of the o-amino ketone, which then isomerizes to the p-amino ketone. In support of this is the fact that we were unable to show the presence of acetyl chloride as a reaction component when we ran the experiment by the earlier described method [4], and also the fact that o-aminoacetophenone when fused with $ZnCl_2$ gives flavaniline [11], which it is impossible to depict without previous rearrangement of the former into p-aminoacetophenone.

EXPERIMENTAL

1. p-Aminoacetophenone and flavaniline from acetanilide. First 20-25 g of freshly fused $ZnCl_2$ was heated at 220-230° for 1 hour; then 10 g of acetanilide was added in 8-10 portions, and the mixture kept at the same temperature for another 15-20 minutes. The usual treatment [2, 4] gave 0.4 g (4.6%) of flavaniline, b.p. 133-141° (15 mm), m.p. 94-95°, acetyl derivative – m.p. 161-163°, reaction for carbonyl group negative, and 1.0 g (10%) of p-aminoacetophenone, b.p. 175-190° (15 mm), m.p. 105-107°. M.p. of the 2,4-nitrophenylhydrazone [12], 259-261°.

2. 2-Amino-5-methylacetophenone from aceto-p-toluidide. To a mixture of 12 g of $AlCl_3$ and 9.2 g of $ZnCl_2$ was added 10 g of aceto-p-toluidide. Separation was made by steam-distillation. We obtained 1.0 g (10%) of 2-amino-5-methylacetophenone, b.p. 235-265°, m.p. 43° (from [13], m.p. 50°, and from [14], m.p. 41-42°); the 2,4-dinitrophenyldydrazone has m.p. 235°. The use of $AlCl_3$ as the catalyst leads to almost solid resinification, while the use of $ZnCl_2$ yields the cyclization product of two molecules of the amino ketone.

3. 2-Chloro-5-methylacetophenone from 2-amino-5-methylacetophenone. The diazotization of 2-amino-5-methylacetophenone in HCl solution (d 1.10) gave 2-chloro-5-methylacetophenone in 20% yield, separated from 2-hydroxy-5-methylacetophenone by shaking with 15% NaOH solution, and purified through the 2,4-dinitrophenylhydrazone [15]. The oxime has m.p. 90-91°.

4. 2-Amino-5-methylacetophenone and o-aminoacetophenone by the Gustavson-Friedel-Crafts reaction. To 15 g of aceto-p-toluidide and 39.9 g of $AlCl_3$ in a solution of 200 ml of light benzine, b.p. 80-100° (the reaction does not go in CS_2 or $C_6H_5NO_2$), was added 20 ml of CH_3COBr in 1 hour at mixture boil. After heating for another 5-6 hours the solvent was distilled off, the complex was hydrolyzed, and the free base was steam-distilled. Treatment of the distillate gave 8.5 g of a fraction with b.p. 235-270°, from which 6 g (40%) of 2-amino-5-methylacetophenone crystallized, m.p. 42-43°; 2,4-dinitrophenylhydrazone, m.p. 230-231°. The mixed melting point of the 2,4-dinitrophenylhydrazone from this experiment and Expt. 2 was not depressed.

When the reaction is run under similar conditions with acetanilide there is obtained, together with p-aminoacetophenone, also a small amount of o-aminoacetophenone; the oxime has m.p. 108°.

5. Lepidine from N-ethylacetanilide. A mixture of 24 g of ethylacetanilide, 24 g of $AlCl_3$ and 18.5 g of $ZnCl_2$ was heated in an oil bath at 290° for 1.5 hours. The melt was dissolved in HCl, made alkaline, and steam-distilled. After separation and distillation of the free bases the tertiary amine was precipitated with potassium ferrocyanide [16], then recovered, and distilled. The fraction with b.p. 250-270° was collected. The picrate has m.p. 209°. The yield of lepidine was 1.5 g (7%).

SUMMARY

1. It was established that the use of aluminum chloride and zinc chloride as catalysts makes it possible to obtain ortho rearrangement of acetylated arylamines.

2. It was established that it is possible to form o-amino ketones by the Gustavson-Friedel-Crafts reaction.

3. Lepidine was obtained by the ortho-rearrangement of N-ethylacetanilide under the influence of aluminum chloride.

4. The mechanism for the rearrangements of acetylated arylamines using $ZnCl_2$ is different from the mechanism using $AlCl_3$.

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REDUCTION OF NAPHTHOLCARBOXYLIC ACIDS

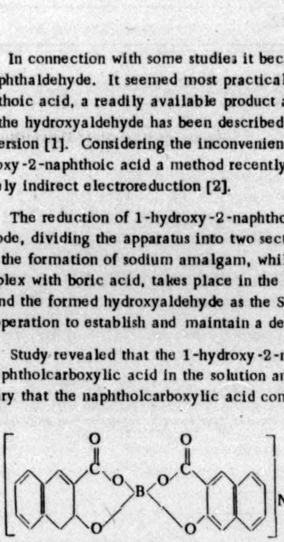
I. PREPARATION OF 1-HYDROXY-2-NAPHTHALDEHYDE

L.N. Lavrishcheva, N.M. Przhiyalgovskaya, S.A. Voitkevich
and V.N. Belov

In connection with some studies it became necessary for us to develop a convenient synthesis of 1-hydroxy-2-naphthaldehyde. It seemed most practical to us to obtain this hydroxyaldehyde from the corresponding hydroxynaphthoic acid, a readily available product at the present time. The conversion of 1-hydroxy-2-naphthoic acid into the hydroxyaldehyde has been described in a series of studies by Weil, who used sodium amalgam for the conversion [1]. Considering the inconvenience of working with sodium amalgam, we used for the reduction of 1-hydroxy-2-naphthoic acid a method recently described for the preparation of salicylaldehyde from salicylic acid, namely indirect electroreduction [2].

The reduction of 1-hydroxy-2-naphthoic acid was run in an electrolyzer in which mercury was used as the cathode, dividing the apparatus into two sections. The electrolysis of caustic takes place in one of the sections with the formation of sodium amalgam, while the reduction of 1-hydroxy-2-naphthoic acid, which is added as a complex with boric acid, takes place in the second section. p-Toluidine is added to the same section in order to bind the formed hydroxyaldehyde as the Schiff base, while hydrochloric (or boric) acid is gradually added during operation to establish and maintain a definite acidity in the solution.

Study revealed that the 1-hydroxy-2-naphthaldehyde yield is strongly influenced by both the concentration of naphtholcarboxylic acid in the solution and the pH of the medium. To obtain a good yield (55-65%) it is necessary that the naphtholcarboxylic acid complex with boric acid be completely dissolved in the solution and that the medium show weakly acid to litmus.



(I)

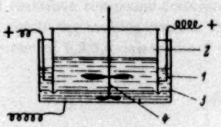
The naphtholcarboxylic acid complex with boric acid apparently has the structure of (I), and can be isolated and obtained in crystalline form in the same manner as the boric acid-salicylic acid complex [3].

EXPERIMENTAL

The electrolyzer, shown in the figure, was assembled as follows: a glass crystallizing dish 1, having a diameter of 160-170 mm and a height of 110 mm, was filled with pure mercury to a height of 25 mm, and then an open glass cylinder 2, having a diameter of 120 mm and a height of 150 mm, was fastened in such manner that one end nearly touched the bottom of the crystallizing dish. Mercury served as the cathode, and also as a seal, separating the two solutions: the caustic solution (20-25%) contained in the collar portion 3 and the naphtholcarboxylic acid solution contained in the cylinder. A nickel plate, immersed in the caustic solution, served as the anode. The apparatus was equipped with a two-blade stirrer 4, the lower blade serving to stir the mercury, and the upper blade to stir the solution being reduced. Direct current (I = 4-5 amp; current density 4 amp/sq. dm) was used to electrolyze the alkali, as a result of which sodium (or potassium) amalgam was formed at the mercury cathode, and then transferred by agitation into the reaction section of the apparatus. The results of a number of experiments, run by us under various conditions, are given in the table. We describe one of the experiments (Expt. 6 in the the table) in greater detail below.

Expt. Nos.	Taken for reaction					Reaction conditions			Yield of hydroxyaldehyde			Recovered unreduced hydroxy acid (in g)
	hydroxynaphthoic acid (in g)	Na_2CO_3 (in g)	H_3BO_3 (in g)	p-toluidine (in g)	H_2O (in ml)	concentration of hydroxy acid (in mole/liter)	quantity of current (in ampere-hrs)	acidification (in g)	g	in % of hydroxy acid taken	based on the current (in %)	
1	14	12	30	12	250	0.3	12	70	1.3	12	3.4	6
2	14	12	30	12	250	0.3	16.5	100	2.35	18		
3	7	6	15	6	250	0.15	11	85	2.6	40		1.6
4	7	6	15	6	250	0.15	11	85	2.5	40		
5	14	12	23	12	500	0.15	11	115	5.8	45	16.5	3
6	10	8	20	8	500	0.1	11	80	5.7	62		
7	10	8	20	8	500	0.1	11	80	5.85	63		
8	7	6	15	6	500	0.08	8.3	80	4.25	66	14.6	
9	7	6	15	6	500	0.08	11	80	4.0	62	10.4	
10	15	12	23	12	750	0.1	11	110	7.85	57	22.4	
11	10	8	30	8	500	0.1	11	100 ml 12% HCl (by drops)	5.1	55		1
12	10	8	5	8	500	0.1	11	150 ml 6% HCl (by drops)	4	44		1.5

Ten grams of 1-hydroxy-2-naphthoic acid was dissolved in soda solution (8 g Na_2CO_3 in 500 ml water) and then 20 g of boric acid was added. The solution was poured into the reaction section of the electrolyzer and then 8 g of finely divided p-toluidine was added with stirring. The direct current (5 amp) was turned on and the electrolysis was run with stirring for 2 hours at 20°. The medium was maintained weakly acid in this experiment by the periodic addition of boric acid (~80 g), with constant checking of the medium pH using litmus paper. Within 15 minutes after the start of reduction the reaction mixture turned yellow, due to formation of the Schiff base. Stirring was continued for another 0.5 hour after turning the current off (after 2 hours), and then the reaction mixture was siphoned into a flask. The Schiff base was separated and treated with 50 ml of dilute sulfuric acid, at the same time removing the liberated hydroxyaldehyde by steam-distillation.



The 1-hydroxy-2-naphthaldehyde separates from the water distillate as greenish-yellow crystals. Yield 5.7 g (62%). After recrystallization from alcohol, m.p. 55-56°. According to [4]: m.p. 59-60°.

Found %: C 76.97, 76.82; H 4.87, 4.75. $C_{11}H_8O_2$. Calculated %: C 76.73; H 4.69.

Oxime – tan needle crystals (from benzene), m.p. 146-147°. From [4]: m.p. 145°.

SUMMARY

1. A method was developed for the indirect electroreduction of 1-hydroxy-2-naphthoic acid to 1-hydroxy-2-naphthaldehyde. Under certain conditions the yield of the hydroxyaldehyde reaches 55-65%. The method is a convenient way of preparing the aldehyde.

2. It was established that the yield of 1-hydroxy-2-naphthaldehyde depends to a large degree on the concentration of the 1-hydroxy-2-naphthoic acid (used as a complex sodium salt of a boric acid-naphtholcarboxylic acid mixture) and on the pH of the medium.

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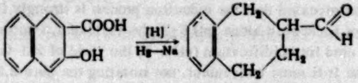
REDUCTION OF NAPHTHOLCARBOXYLIC ACIDS

II. SYNTHESIS OF 2,3-TETRALONECARBOXYLIC ACID AND ITS DECOMPOSITION TO β-TETRALONE

N.M. Przhiyalgovskaya, L.N. Lavrishcheva and V.N. Belov

In the first communication [1] we had shown that the reduction of 1,2-naphtholcarboxylic acid in weakly acid medium with the sodium amalgam obtained electrolytically during reaction is a convenient method for the preparation of 1,2-naphtholaldehyde. In the present study we ran the reduction of the isomeric 2,3-naphtholcarboxylic acid under similar conditions. In this case, together with the corresponding hydroxyaldehyde, we obtained an oily product, showing characteristic aldehyde reactions (silver mirror formation, reduction of Fehling solution), but insoluble in alkalies. When heated with alkali solution the substance becomes quite tarry.

The formation of a similar product in the reduction of 2,3-naphtholcarboxylic acid was observed earlier [2] by Weil and coworkers. The reduction was run with sodium amalgam, obtained from sodium and mercury. The described compound corresponded to ours not only in the earlier mentioned properties and elemental analysis, but also in the melting point of the phenylhydrazone (see the table). The authors assigned this compound the structure of 1,2,3,4-tetrahydro-2-naphthaldehyde.



However, in some respects (see table) this substance is quite different from the 1,2,3,4-tetrahydro-2-naphthaldehyde, described in recent years [3, 4]. This circumstance caused us to make a more detailed study of the properties of the carbonyl compound obtained by us, and also of the conditions for its formation in the reduction of 2,3-naphtholcarboxylic acid. We were able to isolate from the reaction mixture a colorless crystalline product, which from all of the data is β-tetralonecarboxylic acid (1,2,3,4-tetrahydro-2-keto-3-naphthoic acid). This previously unknown β-keto acid decomposes with the liberation of CO_2 and the formation of β-tetralone when heated to 110-113°.

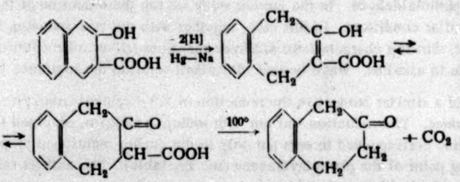
It was unequivocally established by us that the β-tetralone, formed in the decomposition of the β-keto acid isolated by us, is identical with the carbonyl compound, obtained directly in the reduction of 2,3-naphtholcarboxylic acid under the above indicated conditions. All of the crystalline derivatives obtained by us for both of these specimens had the same melting points and failed to show mixed melting point depressions. The identity of these derivatives with the corresponding derivatives of the β-tetralone, obtained by the method of [8], was also established by the mixed melting point test.

As a result, it can be considered proven that the carbonyl compound, obtained in the reduction of 2,3-naphtholcarboxylic acid with sodium amalgam, is β-tetralone. The erroneous conclusion of Weil and others [2], assuming for this compound the structure of 1,2,3,4-tetrahydro-2-naphthaldehyde, was apparently based on the fact that it shows certain properties, characteristic for aldehydes (the difference in the elemental composition for the tetrahydronaphthaldehyde and the tetralone is only several tenths of a percent). It was established by us that also the β-tetralone, obtained by the method of [8], reduces ammoniacal silver oxide solution and Fehling solution.

On the basis of the obtained data the reduction of 2,3-naphtholcarboxylic acid with sodium amalgam in

Derivative	"Tetrahydronaphthaldehyde" of Weil [2]	Our carbonyl compound (β-tetralone)	β-Tetralone from β-tetralonecarboxylic acid	Literature data for: β-tetralone	Literature data for: 1,2,3,4-tetrahydro-2-naphthaldehyde
		Melting point			
Oxime	–	88- 88.2°	87- 88.5°	86.5- 87.5° 89° [6]	–
Phenylhydrazone	106°	106-107°	106-107°	107° [6]	–
2,4-Dinitrophenylhydrazone	–	147-148°	145-146°	–	199-200° [3]
Semicarbazone	–	193-194°	192-193°	190 -191° [6]	194.8-196.8° [5]
		n_D^{20} for the carbonyl compound			
	–	1.5600	1.5598	1.5594 [7]	1.5002 [4]

weakly acid medium can be depicted by the following scheme.



Further study of this reaction revealed that the reduction process is strongly influenced by the pH of the medium. Thus, in the presence of boric acid alone (pH 6-7) the yield of 2,3-tetralonecarboxylic acid is 60-65%. When dilute hydrochloric acid is used for acidification (pH 5-7) the yield of 2,3-tetralonecarboxylic acid drops to 52%. To obtain the β-tetralone it is more convenient, not isolating the pure 2,3-tetralonecarboxylic acid, to decompose the mixture of keto acid and boric acid directly. In this case the β-tetralone yield is respectively (acidification with boric acid or with hydrochloric acid) 60 and 45-50%, based on taken 2,3-naphtholcarboxylic acid. In general the reduction does not go when the reaction is run in hydrochloric acid medium (pH 3-4).

It was also established that the presence of small amounts of boric acid is a necessary reaction condition.* Thus, the reduction in weak acetic acid medium without the addition of boric acid leads to the formation of a resinous mass, which after solidification and grinding gives a powdery product, melting in the range 120-130°. This product represents a mixture of substances, in which the presence of 2,3-tetralonecarboxylic acid could not be shown.

EXPERIMENTAL

Preparation of β-tetralonecarboxylic acid. The reduction was run in the earlier described apparatus [1]. A solution of 10 g of 2,3-naphtholcarboxylic acid, 10 g of soda and 25 g of boric acid in 500 ml of water was placed in the inside glass tube of the electrolyzer, the stirrer was turned on, and a current of 5.5 amps with a voltage of 18 v was passed through. During reaction the temperature was maintained at 18-20°. The alkali, formed from the decomposition of the amalgam, was bound during reduction with either boric acid (about 50 g) or 18% hydrochloric acid (90-130 ml). A weakly acid medium was maintained by checking with litmus paper. After 2 hours the current was turned off, and the mass was stirred for 30 minutes longer. Then the reaction mass was removed from the electrolyzer, filtered from unreacted 2,3-naphtholcarboxylic acid (1-2 g), and acidified with 30% sulfuric acid to strong acidity. The obtained white precipitate (mixture of β-tetralonecarboxylic acid and boric acid) was filtered, washed with water, and dried at 30-40°. The dry precipitate was treated twice with hot benzene (100 ml portions) and rapidly filtered. Cooling of the benzene solution gave β-tetralonecarboxylic acid as fine cream-colored crystals with m.p. 110° (decomposition). Yield 6 g (60%) when operating with boric acid alone and 5.2 g (52%) when acidification is with hydrochloric acid. Recrystallization from benzene gave β-tetralonecarboxylic acid as tiny white crystals with m.p. 113° (decomposition).

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*This is apparently due to the formation of a complex sodium salt of the boric acid-naphtholcarboxylic acid mixture (see [1]).

Found %: C 69.17, 69.35; H 5.31, 5.40; acid number 272.7, 289.5. $C_{11}H_{10}O_3$. Calculated %: C 69.47; H 5.26; acid number 294.2.

All attempts to obtain derivatives of 2,3-tetralonecarboxylic acid involving the keto group led to the formation of β-tetralone derivatives. The ketone content, determined by oximation, was 111%. The high result is explained by the difficulty of titrating the colored mass.

Decomposition of 2,3-tetralonecarboxylic acid to β-tetralone. Three grams of 2,3-tetralonecarboxylic acid was heated to 140° in a small flask fitted with an outlet tube. The evolved gas was passed through a flask containing barium hydroxide solution. A turbidity here indicated the liberation of CO_2. The dark liquid remaining in the flask was vacuum-distilled. All of the substance distilled; b.p. 104-106° (4 mm), n_D^{20} 1.5598. For β-tetralone, b.p. 111-115° (5 mm) [9], n_D^{20} 1.5594 [7].

Oxime. Lustrous, colorless, scale crystals with m.p. 87-88.5°. From [6]: m.p. 86.5-87.5°, 89°.

Phenylhydrazone. Handsome crystals with a mother-of-pearl luster, m.p. 106-107° (from alcohol). From [6]: m.p. 107°.

Found %: N 11.89, 12.00. $C_{16}H_{16}N_2$. Calculated %: N 11.86.

2,4-Dinitrophenylhydrazone. Fine yellow-orange crystals, m.p. 145-146° (from alcohol).

Found %: N 17.09, 17.23. $C_{16}H_{14}O_4N_4$. Calculated %: N 17.17.

Semicarbazone. Fine white crystals (from alcohol), m.p. 192-193° (with rapid heating). From [6]: m.p. 190-191°.

Preparation of β-tetralone. Ten grams of 2,3-naphtholcarboxylic acid was reduced with sodium amalgam, as described above. The mixed precipitate of β-tetralonecarboxylic acid and boric acid was immediately steam-distilled. Here the β-keto acid was decarboxylated, while the β-tetralone collected in the receiver as a pale yellow oil. The oil was extracted with ether, and the ether extracts dried over fused sodium sulfate. The ether was removed by distillation, and the residual oil was vacuum-distilled. B.p. 89-90° (0.4 mm), n_D^{20} 1.5600. The β-tetralone yield when operating with boric acid alone was 60%, and 45-50% when acidification was with hydrochloric acid, in both cases based on taken 2,3-naphtholcarboxylic acid. M.p. of the oxime 88-88.2°, of the phenylhydrazone 106-107°, of the 2,4-dinitrophenylhydrazone 147-148°, and of the semicarbazone 193-194°. The identity of these derivatives with the corresponding derivatives of the β-tetralone, obtained by the method of [8], was established by the method of mixed melting point determinations.

SUMMARY

1. The reduction of 2,3-naphtholcarboxylic acid with electrolytically obtained sodium amalgam was studied in weakly acid medium in the presence of boric acid.

2. It was shown that 1,2,3,4-tetrahydro-2-keto-3-naphthoic acid (previously unknown) is obtained in 60-65% yield under these conditions. When heated to 110-113° this keto acid decomposes to give β-tetralone.

3. It was established that the yield of 2,3-tetralonecarboxylic acid depends on the pH of the medium.

4. A new method was proposed for the preparation of β-tetralone from 2,3-naphtholcarboxylic acid in 60% yield, based on taken acid.

5. It was established that the compound described by Weil and others [2] as being 1,2,3,4-tetrahydro-2-

naphthaldehyde is actually β-tetralone.

6. A scheme was proposed for the reduction of 2,3-naphtholcarboxylic acid with sodium amalgam in acid medium.

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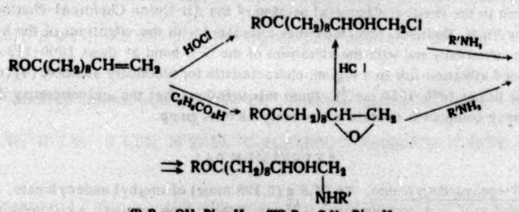
SYNTHESIS OF MERCAPTOAMINO COMPOUNDS

I. SYNTHESIS OF 11-AMINO-10-HYDROXYUNDECANOIC ACID AND RELATED COMPOUNDS

Yu. V. Markova, K. K. Kuzmina and M. N. Shchukina

The purpose of the present study was to obtain 11-amino-10-hydroxyundecanoic acid (I) and some of its derivatives, representing interest as starting substances for the synthesis of the corresponding mercaptoamino compounds. We proposed to synthesize these compounds by the following route.



(I) R = OH, R' = H   (III) R = C_6H_5, R' = H
(II) R = OCH_3, R' = H   (IV) R = C_6H_5, R' = CH_3

The treatment of undecylenic acid with sodium hypochloride by the Bauer method [1] gave 11-chloro-10-hydroxyundecanoic acid, which when treated with aqueous ammonia solution was converted into 11-amino-10-hydroxyundecanoic acid. The obtained aminohydroxyundecanoic acid has only one molecule of crystallization water, which it loses at 120°. The structure of this acid was established on the basis of a spectrographic study of the starting chlorohydroxyundecanoic acid. Bauer and coworkers [1], who described the preparation and properties of the chlorohydroxyundecanoic acid, did not reach a final conclusion as to its structure, but on the basis of the general rule for the addition of hypochlorite to unsaturated compounds, they postulated that 11-hydroxy-10-chloroundecanoic acid is formed in this reaction. The 11-amino-10-hydroxyundecanoic acid obtained by us from the chlorohydroxyundecanoic acid proved to be identical with the acid obtained by the method of [2] from undecylenic acid through the 11-bromo-10-hydroxyundecanoic acid. Consequently, the acid described by Bauer must be considered to be 11-chloro-10-hydroxyundecanoic acid.

11-Chloro-10-hydroxyundecanoic acid, as well as 1-chloro-2-hydroxy-10-benzoyldecane, and also the oxides corresponding to these compounds, were subjected to transformations for the purpose of obtaining the methyl ester of 11-amino-10-hydroxyundecanoic acid and 1-amino-2-hydroxy-10-benzoyldecane.

The methyl ester of 11,10-epoxyundecylenic acid, as well as 10-benzoyl-1,2-decane oxide, were synthesized by the oxidation of the corresponding unsaturated compounds with perbenzoic acid in chloroform solution. Yields of 68 and 77% (respectively) were obtained by using an 8-fold excess of perbenzoic acid. Levy and coworkers [3] used a 100% excess of perbenzoic acid in the oxidation of methyl undecylenate, and a 10% excess in the oxidation of 10-benzoyl-1,2-decene, but they failed to give the yields of the oxides, which, according to our data, are slight under these conditions.

The methyl ester of 11,10-epoxyundecylenic acid and 10-benzoyl-1,2-decene oxide when treated with an ether solution of hydrogen chloride were converted quantitatively into the methyl ester of 11-chloro-10-hydroxyundecanoic acid and 1-chloro-2-hydroxy-10-benzoyldecane, respectively. The heating of these compounds in sealed tubes with a 25-fold excess of aqueous, aqueous-alcohol, or alcoholic ammonia solution at various temperatures (80, 100 and 150°) gave, judging by the analysis data, a mixture of the corresponding primary and secondary hydroxy amines. Repeated recrystallization of the reaction product of 1-chloro-2-hydroxy-10-benzoyldecane with ammonia from alcohol, and then from chloroform, gave a compound which, based on the analysis data, corresponds to the formula $C_{34}H_{51}O_4N$, and is di-(10-benzoyl-2-hydroxydecyl)-amine. We failed to isolate any individual substances from the products obtained in the reaction of the methyl ester of 11-chloro-10-hydroxyundecanoic acid with ammonia.

Similar results were obtained in the reaction of ammonia with the oxides: methyl 11,10-epoxyundecylenate and 10-benzoyl-1,2-decene oxide. Repeated recrystallization of the reaction product, obtained in the heating of 10-benzoyl-1,2-decene oxide with either excess aqueous or aqueous-alcoholic ammonia in a sealed tube at 150°, also gave di-(10-benzoyl-2-hydroxydecyl)-amine.

The heating of 1-chloro-2-hydroxy-10-benzoyldecane with excess methylamine in alcohol solution at 120° in a sealed tube gave 1-N-methylamino-2-hydroxy-10-benzoyldecane hydrochloride, and this on treatment with alkali gave 1-N-methylamino-2-hydroxy-10-benzoyldecane (IV).

The structure of the obtained compounds was decided on the basis of spectrographic studies. The spectra of the chlorohydroxyundecanoic acid, methyl ester of the chlorohydroxyundecanoic acid and chlorohydroxy-10-benzoyldecane, taken in the Physical-Chemical Section of the All-Union Chemical-Pharmaceutical Scientific-Research Institute by Yu.N. Sheinker, revealed bands associated with the vibrations of the hydroxyl group at about 3500 cm^{-1} (valence vibrations) and with the vibrations of the C–O bond at about 1000-1120 cm^{-1}. The frequency value of the C–O bond vibration lies in a region, characteristic for secondary alcohols [4] (the frequency value for primary alcohols lies at 1075-1110 cm^{-1}). From this it follows that the aminohydroxy derivatives obtained from the chlorohydroxy compounds contain a secondary alcohol group.

EXPERIMENTAL

Methyl 11,10-epoxyundecylenate. To 24.8 g (0.125 mole) of methyl undecylenate, dissolved in 50 ml of chloroform, was added at 0° in 4 portions (each 0.250 mole) at 3 hour intervals a chloroform solution of active perbenzoic acid, after which the reaction solution was placed in the refrigerator at −2 to 0° overnight. The next day the solution was washed with 10% sodium hydroxide, then with water, and dried over fused sodium sulfate. After removal of the solvent the residue was vacuum-distilled. Distillation at 25 mm gave two fractions with b.p. 158-168°, 3.9 g; and 168-174°, 15.9 g. Titration of weighed samples of the obtained fractions with an ether solution of hydrogen chloride gave the oxide content of the 1st fraction as 70%, and of the 2nd as 100%. As a result, the yield of methyl 11,10-epoxyundecylenate was 18.2 g (67.9%).

10-Benzoyl-1,2-decene oxide. A solution of 30.5 g (0.125 mole) of 10-benzoyl-1,2-decene in 100 ml of chloroform was treated with a chloroform solution of perbenzoic acid under the conditions of the preceding experiment. Vacuum-distillation at 15 mm gave fractions with b.p. 215-225°, 2 g; 225-231°, 22.4 g and 231-240°, 4.5 g. Analysis of the obtained fractions gave a respective oxide content of 60, 92 and 75%. The yield of oxide was 25 g (76.7%). The substance is a thick, slightly colored liquid, crystallizing rapidly on standing. M.p. 37°. It is soluble in the usual organic solvents, and difficultly soluble in petroleum ether.

1-Chloro-2-hydroxy-10-benzoyldecane. A solution of 5.2 g of 10-benzoyl-1,2-decene oxide (5.7 g of 92% material) in 30 ml of absolute ether was treated with a solution of 1.1 g of hydrogen chloride in 150 ml of absolute ether and the mixture allowed to stand for 2 hours at room temperature. After removing the ether the residue (5.8 g) was recrystallized several times from a mixture of ether and petroleum ether (1 : 4). Colorless crystals with m.p. 62-64°, readily soluble in chloroform, ether and alcohol, and insoluble in water and petroleum ether.

Found %: C 68.98; H 8.38; Cl 11.99. $C_{17}H_{25}O_2Cl$. Calculated %: C 68.78; H 8.49; Cl 11.94.*

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*All of the analyses were run in the Microanalysis Laboratory of the Institute under the direction of V.V. Kolpakov.

Methyl 11-chloro-10-hydroxyundecanoate. To 4.3 g (0.02 mole) of methyl 11,10-epoxyundecylenate was added 180 ml of an ether solution of hydrogen chloride (1.1 g HCl – 0.03 mole). After 2 hours the ether was distilled off, and the residue was vacuum-distilled. B.p. 200-202° at 20 mm; m.p. 38-41°. The yield was quantitative (5 g). The substance is soluble in the usual organic solvents, and insoluble in water.

Found %: C 57.85; H 9.21; Cl 13.90. $C_{12}H_{23}O_3Cl$. Calculated %: C 57.48; H 9.19; Cl 14.17.

11-Amino-10-hydroxyundecanoic acid. A mixture of 2.36 g of 11-chloro-10-hydroxyundecanoic acid [1] and 250 ml of aqueous (25%) ammonia solution was stirred for 24 hours at room temperature. The reaction solution was evaporated, and the substance separating here was filtered and washed with water. Yield 1.9 g (90%). After two recrystallizations from water and drying in a vacuum-desiccator over phosphorus pentoxide the substance melted at 193.5-195° (with cleavage of water), and after drying at 120° it melted at 199-200°. The substance, dried over phosphorus pentoxide, was taken for analysis.

Found %: C 55.91; H 10.54; N 5.88; H_2O (120°) 7.73. $C_{11}H_{23}O_3N \cdot H_2O$. Calculated %: C 56.14; H 10.70; N 5.95; H_2O 7.65.

The mixed melting point with the 11-amino-10-hydroxyundecanoic acid, obtained by the method of [2], was not depressed.

Hydrochloride – colorless crystals with m.p. 127-128°, readily soluble in water and alcohol.

Found %: C 52.55; H 9.43; N 5.50; Cl 13.86. $C_{11}H_{24}O_3NCl$. Calculated %: C 52.35; H 9.53; N 5.50; Cl 13.95.

Hydrobromide – colorless crystals with m.p. 119-121°, soluble in alcohol and water.

Found %: C 43.88; H 8.15; N 4.68; Br 26.59. $C_{11}H_{24}O_3NBr$. Calculated %: C 44.29; H 8.05; N 4.71; Br 26.80.

Reaction of 10-benzoyl-1,2-decene oxide with ammonia. A mixture of 3 g of the oxide and 40 ml of 33% aqueous ammonia solution was heated in a sealed tube at 150° for 8 hours. The obtained precipitate was filtered, washed with water, and dried in a vacuum-desiccator (0.9 g). After 2 recrystallizations from alcohol, then from chloroform, a small amount of di-(10-benzoyl-2-hydroxydecyl)-amine was obtained. M.p. 116-118°. The substance is soluble in alcohol and chloroform, and insoluble in water and ether.

Found %: C 75.79; H 9.50; N 2.77. $C_{34}H_{51}O_4N$. Calculated %: C 75.87; H 9.55; N 2.60.

Reaction of 1-chloro-2-hydroxy-10-benzoyldecane with ammonia. A mixture of 1.5 g of 1-chloro-2-hydroxy-10-benzoyldecane and 25 ml of 33% aqueous ammonia solution was heated in a sealed tube at 150° for 8 hours. The substance was purified in the same manner as described above. We obtained 0.2 g of di-(10-benzoyl-2-hydroxydecyl)-amine. M.p. 116-118°. The mixed melting point of this substance with the same substance, obtained from the corresponding oxide, was not depressed.

1-N-Methylamino-2-hydroxy-10-benzoyldecane. A mixture of 1.5 g of 1-chloro-2-hydroxy-10-benzoyldecane and 20 ml of 18% alcoholic methylamine solution was heated in a sealed tube at 120° for 8 hours. At the end of reaction the solvent was vacuum-distilled, and the residue was repeatedly washed with ether. We obtained 1.3 g of substance with m.p. 75-80°. The substance contains chloride ion, and is readily soluble in water and alcohol; it hydrolyzes when dissolved in water. Treatment of the obtained 1-N-methylamino-2-hydroxy-10-benzoyldecane hydrochloride with aqueous caustic solution gave the corresponding free base. After recrystallization from aqueous alcohol – colorless crystals with m.p. 78-80.5°.

Found %: C 74.30; H 9.68; N 4.53. $C_{18}H_{29}O_2N$. Calculated %: C 74.18; H 10.03; N 4.80.

SUMMARY

1. Methyl 11-chloro-10-hydroxyundecanoate and 1-chloro-2-hydroxy-10-benzoyldecane were obtained from the corresponding epoxides, for which methods to obtain them in high yields were developed.

2. 11-Amino-10-hydroxyundecanoic acid was obtained, from the corresponding chlorohydroxyundecanoic acid, and we also synthesized 1-N-methylamino-2-hydroxy-10-benzoyldecane and di-(10-benzoyl-2-hydroxydecyl)-amine.

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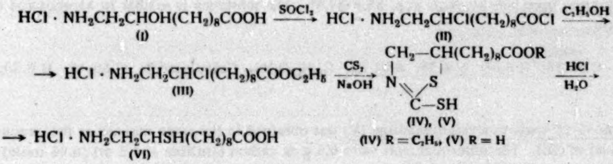
SYNTHESIS OF MERCAPTOAMINO COMPOUNDS

II. SYNTHESIS OF 11-AMINO-10-MERCAPTOUNDECANOIC ACID AND RELATED COMPOUNDS

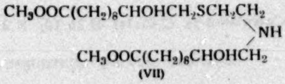
Yu.V. Markova, K.K. Kuzmina and M.N. Shchukina

Aminomercaptans of the type $COOH(CH_2)_nCHSHCH_2NH_2$ have been studied very slightly, although they, as analogs of β-mercaptoethylamine and cysteine, could undoubtedly be of interest for biological testing. In this paper we describe the synthesis of a new compound of this type – 11-amino-10-mercaptoundecanoic acid hydrochloride, and also of other similar undecanoic acid derivatives. The synthesis of 11-amino-10-mercaptoundecanoic acid hydrochloride was accomplished by the following scheme


HCl · NH₂CH₂CHOH(CH₂)₈COOH
(I)
SOCl₂
HCl · NH₂CH₂CHCl(CH₂)₈COCl
(II)
C₂H₅OH
HCl · NH₂CH₂CHCl(CH₂)₈COOC₂H₅
(III)
CS₂
NaOH
CH₂—CH(CH₂)₈COOR
N
S
C—SH
(IV), (V)
HCl
H₂O
HCl · NH₂CH₂CHSH(CH₂)₈COOH
(VI)
(IV) R = C₂H₅, (V) R = H

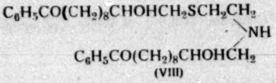
Treatment of 11-amino-10-hydroxyundecanoic acid hydrochloride (I) [1] with thionyl chloride gave the acid chloride of 11-amino-10-chloroundecanoic acid hydrochloride (II), which when heated with anhydrous ethyl alcohol was converted into the aminochloroundecanoic acid ethyl ester hydrochloride (III). The latter with carbon bisulfide in the presence of alkali was transformed into 2-mercapto-5-(8-carbethoxyoctyl)-thiazoline (IV), or if a large excess of alkali is used in the reaction, into 2-mercapto-5-(8-carboxyoctyl)-thiazoline (V). Hydrolysis occurs when either (IV) or acid (V) is heated with concentrated hydrochloric acid in a sealed tube at 150°, and here 11-amino-10-mercaptoundecanoic acid hydrochloride (VI) was obtained.

The synthesis of aminoethanethio-11-hydroxy-10-undecanoic acid [2] is described in the literature, which was accomplished by reacting β-mercaptoethylamine with 11-bromo-10-hydroxyundecanoic acid or with 10,11-epoxyundecylenic acid. It seemed of interest to run similar reactions with the methyl ester of 10,11-epoxyundecylenic acid and with 10-benzoyl-1,2-decene oxide [1]. The shaking of these two oxides with β-mercaptoethylamine in aqueous medium at room temperature for many hours gave compounds, which, based on the analysis data, had the structural formulas $C_{26}H_{51}O_6NS$ and $C_{36}H_{55}O_4NS$, respectively. The composition of the obtained compounds shows that they were formed as the result of two oxide molecules condensing with one β-mercaptoethylamine molecule. Proceeding from the fact that the oxide of undecylenic acid [3], the same as other unsymmetrical α-oxides, adds amines and mercaptans in such manner that a secondary alcohol group is formed, it can be postulated that the compounds corresponding to the above empirical formulas have the structure of (VII) and (VIII), respectively.



$$\begin{matrix} CH_3OOC(CH_2)_8CHOHCH_2SCH_2CH_2 \\ \qquad\qquad\qquad\qquad\qquad\qquad NH \\ CH_3OOC(CH_2)_8CHOHCH_2 \end{matrix}$$

(VII)



$$\begin{matrix} C_6H_5CO(CH_2)_8CHOHCH_2SCH_2CH_2 \\ \qquad\qquad\qquad\qquad\qquad\qquad NH \\ C_6H_5CO(CH_2)_8CHOHCH_2 \end{matrix}$$

(VIII)

EXPERIMENTAL

11-Amino-10-chloroundecanoyl chloride hydrochloride (II). A mixture of 10 g of aminohydroxyundecanoic acid hydrochloride [1] and 30 ml of thionyl chloride was stirred for 15-30 minutes at room temperature, and here the precipitate dissolved completely. Stirring of the reaction solution at the same temperature was continued for another 3 hours, and then at 50-60° for 5 hours. A precipitate was obtained when the reaction solution was cooled. To obtain more complete precipitation the reaction mass was treated with absolute ether, and the precipitate filtered and washed several times with ether. Yield 7.4 g (86%). M.p. 117.5-119.5° (with decomposition). The crude hydrochloride was analyzed.

Found %: Cl 35.70. $C_{11}H_{22}ONCl$. Calculated %: Cl 36.59.

Ethyl 11-amino-10-chloroundecanoate hydrochloride (III). A solution of 7 g of (II) in 50 ml of anhydrous ethyl alcohol was boiled for 8 hours. The precipitate obtained on cooling was filtered and recrystallized from anhydrous alcohol. Yield 6.1 g (63%). M.p.133-135°. The substance is soluble in water and alcohol, and insoluble in ether.

Found %: C 52.12; H 8.78; N 5.01; Cl 23.33. $C_{13}H_{27}O_2NCl_2$. Calculated %: C 51.99; H 9.06; N 4.66; Cl 23.61.

2-Mercapto-5-(8-carbethoxyoctyl)-thiazoline (IV). To a solution of 2 g of (III) in 15 ml of water was simultaneously added in drops and with stirring 0.5 g of carbon bisulfide and 2.5 ml of 22% aqueous sodium hydroxide solution. The temperature rose to 35° during reaction, and here the solution became clear after several minutes, and then a precipitate separated. The precipitate was filtered and washed with water. Yield 1.5 g (75%). After recrystallization from 80% alcohol, m.p. 55.5-57.5°. The substance is soluble in alcohol and ether, and insoluble in water.

Found %: C 55.36; H 8.07; N 4.75; S 21.32. $C_{14}H_{25}O_2NS_2$. Calculated %: C 55.40; H 8.30; N 4.61; S 21.13.

2-Mercapto-5-(8-carboxyoctyl)-thiazoline (V) was obtained in the same manner as the preceding from 0.2 g (0.015 mole) of (III). The other reactants were 0.5 g of carbon bisulfide and 5 ml (0.06 mole) of 22% sodium hydroxide solution. Yield 1.4 g (80%). After recrystallization from 80% alcohol the substance had m.p. 139-141°.

Found %: C 52.63; H 7.59; N 5.05; S 23.29. $C_{12}H_{21}O_2NS_2$. Calculated %: C 52.32; H 7.68; N 5.08; S 23.28.

11-Amino-10-mercaptoundecanoic acid hydrochloride (VI). A mixture of 3 g of (IV) and 50 ml of concentrated hydrochloric acid was heated in a sealed tube at 150° for 5 hours. A precipitate separated from the reaction solution when the tube was opened. This was filtered, washed with concentrated hydrochloric acid, and dried in a vacuum-desiccator. Yield of the hydrochloride 1.6 g (50%). After recrystallization from anhydrous ethyl alcohol the substance melted at 139-142°. Soluble in water and alcohol, and insoluble in ether.

Found %: C 49.27; H 8.83; N 5.10; S 11.88; Cl 13.43. $C_{11}H_{24}O_2NSCl$. Calculated %: C 48.97; H 8.96; N 5.19; S 11.88; Cl 13.14.

N,S-[Di-(10-carbomethoxy-2-hydroxydecyl)]-mercaptoethylamine (VII). A mixture of 2.14 g (0.01 mole) of methyl 10,11-epoxyundecylenate [1] and 1.54 g (0.02 mole) of β-mercaptoethylamine [4] in 100 ml of water was shaken at room temperature for 50 hours. The oily precipitate that separated here was filtered, washed with water, and dried in a vacuum-desiccator. After rubbing the dry residue with acetone, followed by washing with ether, we obtained 0.29 g (10%) of substance. M.p. 68-73°.

Found %: C 61.20; H 9.95; N 2.95. $C_{26}H_{51}O_6NS$. Calculated %: C 61.74; H 10.16; N 2.76.

N,S-[Di-(2-hydroxy-10-benzoyldecyl)]-mercaptoethylamine (VIII). A mixture of 2 g of 10-benzoyl-1,2-decene oxide, and 1.2 g of β-mercaptoethylamine in 100 ml of water was shaken at room temperature for 50 hours. The obtained substance was isolated in the same manner as (VII). Yield 0.6 g. After recrystallization from alcohol the substance had m.p. 92-94°.

Found %: C 72.85; H 9.22; N 2.30; S 5.46. $C_{36}H_{55}O_4NS$. Calculated %: C 72.51; H 9.27; N 2.34; S 5.36.

SUMMARY

1. The synthesis of 11-amino-10-mercaptoundecanoic acid was accomplished.

2. The reaction of β-mercaptoethylamine with methyl 10,11-epoxyundecylenate and with 10-benzoyl-1,2-decene oxide gave N,S-[di-(10-carbomethoxy-2-hydroxydecyl)]-mercaptoethylamine and N,S-[di-(2-hydroxy,-10-benzoyldecyl)]-mercaptoethylamine, respectively.

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*Original Russian pagination. See C.B. translation.

SYNTHESES WITH 1,1,3,3-TETRAALKOXYPROPANES

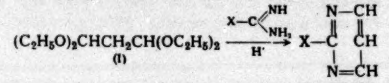
PREPARATION OF THE SIMPLER HETEROCYCLIC COMPOUNDS

T.V. Protopopova and A.P. Skoldinov

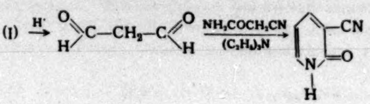
In a previous communication [1] we described a number of 1,1,3,3-tetraalkoxypropanes of general formula $(RO)_2CHCH_2CH(OR)_2$, in their structure being full acetals of malonaldehyde [2]. In this paper we discuss the possibility of utilizing 1,1,3,3-tetraethoxypropane (I) to obtain the simpler heterocyclic compounds by its reaction with nitrogen compounds.

(I) reacts with water solutions of salts of hydroxylamine, hydrazine or semicarbazide even on gentle warming. However, the optimum results were obtained when the reaction was run in the presence of acids, causing saponification of the acetal groups of (I) with the formation of malonaldehyde, appearing as an intermediate product in all of the reactions described below. The use of acid is necessary in the case of reacting (I) with urea or its derivatives.

The reaction of (I) with urea gave 2-hydroxypyrimidine hydrochloride in high yield. It should be mentioned that the reaction of β-ethoxyacrolein diethyl acetal with urea under analogous conditions leads to a condensation product, containing 2 moles of urea per mole of malonaldehyde [3]. (I) also reacts smoothly with thiourea and with guanidine, and here the hydrochlorides of 2-mercaptopyrimidine and 2-aminopyrimidine are obtained, respectively.



As an example of synthesizing pyridine compounds we describe the preparation of 3-cyano-2-pyridone by the reaction of (I) with cyanacetamide. In this case the optimum results were obtained when the second phase of the reaction (cyclization) was run in the presence of triethylamine.



The reaction proceeds in high yield also for the preparation of five-membered heterocycles, and specifically of isoxazole, by the reaction of (I) with hydroxylamine salts,* and of pyrazole [4] (or of the amide of 1-pyrazolecarboxylic acid), by the reaction of (I) with hydrazine salts (or with semicarbazide salts).

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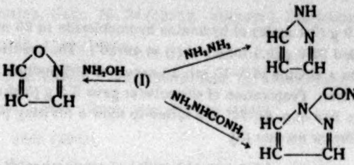
*After the present study had been completed a communication appeared on the preparation of isoxazole, also starting with 1,1,3,3-tetraethoxypropane [5].



The ready availability of the starting materials, the simplicity of the processes and the fully satisfactory yields permit the conclusion that 1,1,3,3-tetraalkoxypropanes can be successfully used for the synthesis of a whole series of heterocyclic compounds.

EXPERIMENTAL

2-Hydroxypyrimidine. To a mixture of 6.1 g (0.1 mole) of urea, 110 ml of ethyl alcohol and 22.0 g (0.1 mole) of 1,1,3,3-tetraethoxypropane (I) was added, with stirring, 20 ml of concentrated hydrochloric acid. The light-yellow reaction solution was allowed to stand overnight, after which the alcohol was removed in vacuo. The residue on cooling deposited white crystals of 2-hydroxypyrimidine hydrochloride, weight 8.0 g, m.p. 198-200° (with decomposition). From [6]: m.p. 200-205° (with decomposition). The mother liquor gave an additional 1.6 g of somewhat less pure substance. Total yield 72%.

Found %: N 21.13, 21.08; Cl 26.54, 26.37. $C_4H_4ON_2 \cdot HCl$. Calculated %: N 21.13; Cl 26.76.

A solution of 10.7 g (0.08 mole) of 2-hydroxypyrimidine hydrochloride in 5 ml of water was treated with a solution of 3.28 g (0.08 mole) of sodium hydroxide in 10 ml of water, the mixture evaporated in vacuo to dryness, and the dry residue extracted with ethyl acetate (0.5 liter). We obtained 6.4 g (83%) of 2-hydroxypyrimidine with m.p. 177-178°.*

Found %: C 50.18, 49.97; H 4.34, 4.34; N 29.00, 29.09. $C_4H_4ON_2$. Calculated %: C 50.00; H 4.20; N 29.16.

2-Mercaptopyrimidine. To a solution of 7.9 g (0.104 mole) of thiourea in 18 ml of concentrated hydrochloric acid was gradually added with stirring 22.0 g (0.1 mole) of (I). The next day the obtained 2-mercaptopyrimidine hydrochloride crystals (2.7 g) were filtered and the mother liquor was evaporated in vacuo to small volume. An additional 10.5 g of hydrochloride was obtained in this manner. Total yield 89%. For analysis the substance was recrystallized from alcohol with the addition of concentrated hydrochloric acid.

Found %: N 18.76, 18.91; Cl 23.96, 23.78. $C_4H_4N_2S \cdot HCl$. Calculated %: N 18.85; Cl 23.90.

A solution of 4.5 g (0.03 mole) of the hydrochloride in 70 ml of 1 N sodium hydroxide solution was treated with 30% acetic acid until acid. Here 2.95 g of 2-mercaptopyrimidine with m.p. 214-215° (with decomposition) was obtained. After recrystallization from water the substance had m.p. 217-218° (with decomposition). From [7]: m.p. 219-220° (with decomposition).

2-Aminopyrimidine. To a solution of 10 g (0.1 mole + 5% excess) of guanidine hydrochloride in 40 ml of water and 25 ml of concentrated hydrochloric acid was added in 1.5 hours, with stirring, 22 g (0.1 mole) of (I), after which the mixture was stirred for another 2 hours and then allowed to stand overnight. The solution was evaporated in vacuo to dryness, the residue treated with 40% sodium hydroxide solution, the obtained mixture dried in a vacuum-desiccator, and then extracted with benzene. We obtained 7.8 g (82%) of 2-aminopyrimidine with m.p. 123-124°, failing to give a melting point depression when mixed with a specimen of the compound, obtained in known manner [8].

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*Literature [6]: m.p. 178-180°. In our first experiments we obtained a substance with m.p. 160-161°, not changing after recrystallization from various solvents. Based on analysis it had the composition of 2-hydroxypyrimidine (isomeric form?). Later the 2-hydroxypyrimidine was obtained only with m.p. 177-178°, in which connection the earlier obtained low-melting form when seeded with the high-melting form was converted into the latter.

Pyrazole. To a solution of 7.0 g (0.1 mole) of hydrazine hydrochloride in 20 ml of water and 5 ml of 1 N hydrochloric acid was gradually added 22.0 g (0.1 mole) of (I) at 40-50°. The reaction mixture was stirred for 1 hour at 50°, evaporated in vacuo to a volume of 5-10 ml, an excess of 30% sodium hydroxide added, and the mixture repeatedly extracted with ether. Evaporation of the solvent gave 5.5 g (80%) of pyrazole with m.p. 63-65°. After sublimation the substance had m.p. 68-69° and failed to show a melting point depression when mixed with the pyrazole, obtained in a different manner [3].

1-Pyrazolecarboxamide. To a solution of 5.8 g (0.052 mole) of semicarbazide hydrochloride in 20 ml of water was gradually added, with stirring, 11.0 g (0.05 mole) of (I), after which the mixture was stirred at room temperature for another 2.5 hours. The obtained crystals of 1-pyrazolecarboxamide were filtered. Yield 4.15 g (75%), m.p. 140-141° (from alcohol). From [3]: m.p. 136.5°.

Found %: N 37.62, 37.50. $C_4H_5ON_3$. Calculated %: N 37.88.

The heating of the amide with 3 N hydrochloric acid resulted in its saponification and decarboxylation to yield pyrazole with m.p. 66°, failing to depress the melting point when mixed with the specimen, obtained by the method described above.

Isoxazole. To a solution of 7.6 g (0.11 mole) of hydroxylamine hydrochloride in 50 ml of water and 5 ml of 1 N HCl was gradually added 22 g (0.1 mole) of (I) at 50-60°, the reaction mixture heated for 30 minutes on a boiling water bath, and then a mixture of alcohol, isoxazole and water distilled into a receiver, containing a solution of 29 g of cadmium chloride in 25 ml of water. The precipitate of isoxazole-cadmium chloride binary salt was filtered, washed with saturated cadmium chloride solution, and decomposed by boiling with 15 ml of water. The distillate was saturated with sodium chloride to separate the oxazole, while the water layer was redistilled to give an additional amount of isoxazole. The product was dried over magnesium sulfate and then distilled to give 5.0 g (72%) of isoxazole with b.p. 93.5-94.5° (729 mm), d_4^{20} 1.0787. From [9]: b.p. 95-95.5°, d_{14}^{14} 1.0843.

3-Cyano-2-pyridone. A homogeneous solution, obtained by heating (15-20 minutes at 50°) 11.0 g (0.05 mole) of (I) with 20 ml of 0.5 N hydrochloric acid solution, was treated under cooling with triethylamine until distinctly alkaline to litmus (about 8 ml), and then a solution of 4.5 g (0.05 mole) of cyanacetamide in 20 ml of water was added. The reaction mixture was allowed to stand for 2 hours at room temperature, and then it was heated for 2 hours at 60° and on a boiling water bath for 1 hour. The obtained solution was evaporated in vacuo to dryness, the residue treated under cooling with a mixture of anhydrous alcohol and ether (1 : 3), and the resulting light-yellow crystalline precipitate filtered and washed with the same mixture. We obtained 3.45 g (57%) of substance with m.p. 224-225° (from alcohol). From [10]: m.p. 225-226°.

SUMMARY

1. 2-Hydroxy-, 2-mercapto- and 2-aminopyrimidine, pyrazole, 1-pyrazolecarboxamide, isoxazole and 3-cyano-2-pyridone were obtained in high yields by the reaction of 1,1,3,3,-tetraethoxypropane with the corresponding nitrogen compounds.

2. It was shown that the 1,1,3,3-tetraalkoxypropanes are convenient stable malonaldehyde derivatives, liberating the latter at reaction moment in the presence of aqueous acid.

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PREPARATION OF 2,3-DIMERCAPTOPROPANOL, CONTAINING RADIOACTIVE SULFUR

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Among organic sulfur-containing compounds 2,3-dimercaptopropanol, BAL (British Anti-Lewisite) and its derivatives are of considerable interest as prophylactics in the treatment of poisoning from arsenic compounds and many heavy metals. Of all of the described methods for the preparation of dithiols, in the case of 2,3-mercaptopropanol, the direct reaction of a 2,3-dihalopropyl alcohol with either potassium or sodium hydrosulfite gives good results.

$$CH_2SH-CHSH-CH_2OH$$

An important condition of the reaction is the use of a closed system, which permits avoiding the formation of disulfides.

Ing [1] obtained dimercaptopropanol from dichloropropanol in about 50% yield, but the purity of the obtained substance did not exceed 93%. Better results are obtained with dibromopropanol, in which connection heating is not required for the reaction. Thus, Stocken [2] obtained BAL in 64% yield, running the reaction at room temperature. A yield of 80% is indicated in a patent issued to Peters and coworkers [3].

To study the adsorption of dimercaptopropanol by the skin and its rate of elimination from the organism we synthesized the compound, containing radioactive sulfur. Simpson and Young [4] obtained BAL with labeled sulfur from radioactive yperite, hydrogen sulfide, sodium hydrosulfide and the dibromopropanol. The method is extremely tedious. Peters and coworkers [5] started with the radioactive sulfur in barium sulfate, which by reduction with carbon was converted into the sulfide. The sulfide was decomposed with hydrochloric acid, and the liberated radioactive hydrogen sulfide was absorbed in sodium hydroxide. The obtained sodium hydrosulfide solution was mixed with a solution of ammonium hydrosulfide in methyl alcohol and then heated with the dibromopropanol in a sealed ampoule. The dimercaptopropanol with labeled sulfur was obtained in 56% yield. This method cannot be considered perfect, since the heating to 90-95° causes partial decomposition of the dimercaptopropanol, while the use of ammonium hydrosulfide leads to the formation of a by-product, namely dimercaptopropylamine.

In our synthesis of the dimercaptopropanol with radioactive sulfur we used sodium hydrosulfide and the reaction was run at room temperature. Preliminary experiments revealed that reaction between the dibromopropanol and sodium hydrosulfide in either methanolic or ethanolic medium proceeds in good yield (73%) at room temperature in 5-8 days. Necessary reaction conditions are a closed system (thick-walled bottle, completely filled with reaction mixture) and an excess of sodium hydrosulfide (6-8 moles of hydrosulfide per mole of dibromopropanol). However, when working with labeled sulfur the method, successfully used to synthesize the inactive substance, is completely out. Actually, only a part of the radioactive sulfur goes to form the dimercaptopropanol, while the greater portion remains unused and escapes as hydrogen sulfide on acidification. This leads to unproductive consumption of the isotope and reduces the total activity of the obtained dimercaptopropanol considerably. To avoid this, we ran the first stage of the reaction with a 2-fold excess of the dibromopropanol, calculated on the basis of one mole of the hydrosulfide with radioactive sulfur. This assured complete utilization of the radioactive sulfur.

EXPERIMENTAL

Synthesis of dimercaptopropanol containing S^{35}. In our work we used the radioactive sulfur isotope S^{35}, being β-emitting with a half life of ~87 days, in the form of $Na_2S \cdot 9H_2O$. The weighed sample of S^{35}-containing sodium sulfide (410 mg) was placed in a 100-ml cylindrical flask fitted with an escape tube and dropping funnel. Hydrochloric acid (1 : 1) was cautiously added from the funnel in drops, and the evolved hydrogen sulfide was passed into an alcohol solution of sodium ethylate, prepared from 4.2 g of sodium. After the active hydrogen sulfide had ceased to evolve the ethylate solution was saturated with inactive hydrogen sulfide. The alcohol solution of the hydrosulfide was then cooled and mixed with a solution of 50 g of the dibromopropanol in alcohol. The reaction mixture was placed in a thick-walled flask of such volume that it was completely full (volume of the mixture about 150 ml) and then kept at room temperature. After 5 days the flask was unstoppered, the contents mixed with a new portion of sodium hydrosulfide (not containing S^{35}), and the whole transferred to a vessel of larger volume. This second stage of the reaction was run to bind the unreacted dibromopropanol. After another 5 days the reaction mixture was treated with hydrochloric acid until weakly acid to congo, and the liberated hydrogen sulfide was tested for its S^{35} content. A qualitative test confirmed the absence of radioactivity in the excess hydrosulfide, i.e., all of the radioactive sulfur went to form the dimercaptopropanol in the first stage. The aqueous-alcohol solution was filtered from the salt precipitate and concentrated in vacuo in a stream of nitrogen. Distilled water was added to the residue, and the pale yellow oil that separated here was extracted with chloroform. The extract was dried over sodium sulfate, the chloroform was distilled, and the residue was fractionated in vacuo. The yield was 16 g (57%). The compound was a colorless oil with b.p. 64-65° (0.2 mm), n_D^{20} 1.5730, d_4^{20} 1.2500 (the n_D^{20} and d_4^{20} of the purified Oxford compound were respectively 1.5733 and 1.2463 [2]). The S^{35}-containing 2,3-mercaptopropanol synthesized by us was quite pure and its constants did not differ noticeably from those of the nonradioactive compounds, obtained by us earlier, or from those given in the literature.

Study of isotopic exchange of sulfur in the system dimercaptopropanol-sodium hydrosulfide at 37°. Since the presence of exchange at low temperature would render difficult the preparation of a dimercaptopropanol with S^{35}, it was necessary to determine if the isotopic exchange of sulfur takes place in the system dimercaptopropanol-sodium hydrosulfide. We chose 80% alcohol as the medium for the exchange, which assured complete solution of both components. In one series of experiments the radioactive sulfur was contained in the hydrosulfide, and in another series it was contained in the dimercaptopropanol. Sodium hydrosulfide, containing radioactive sulfur, was prepared as follows. Radioactive hydrogen sulfide, obtained from sodium sulfide, was absorbed in an alcoholic solution of caustic. The alcoholic hydrosulfide solution was evaporated in vacuo, cooled, and the hydrosulfide was precipitated by the addition of absolute ether. The exceedingly hygroscopic crystals were washed with cold ether and dried in a desiccator over phosphorus pentoxide. Weighed samples of the dimercaptopropanol and hy-

TABLE 1

Isotopic Exchange of Sulfur Between Sodium Hydrosulfide and Dimercaptopropanol at 37° in Alcohol (S^{35} contained in the hydrosulfide; mixture consisted of 320 mg NaHS and 1.065 g dimercaptopropanol in 100 ml of 80% alcohol)

Time of exchange (in hrs)	Activity of the hydrosulfide in the test sample without a ground (impulses/min)	Absolute static measurement error (impulses/min)
0	2690	30
0.5	2650	30
1	2660	30
2	2560	29
3.5	2670	30
6.0	2640	30
8.5	2560	29
11	2680	30
14	2640	30

drosulfide were dissolved in 80% alcohol, and the solution transferred to a 150-ml flask, which was placed in a thermostat. The experiments were run at 37 ± 0.5° for 14 hours. Two parallel samples were taken, which were analyzed as follows. Five ml of the solution was placed in a small separatory funnel, diluted with water, and the separated dimercaptopropanol extracted with chloroform. The aqueous-alcohol solution of the hydrosulfide was transferred to a small beaker, and the hydrosulfide was oxidized to the sulfate. For this the solution was treated with 0.5 ml of bromine, the mixture heated for 15 minutes, and then 1 ml of concentrated nitric acid was added. The heating was continued until reaction ceased, after which the mixture was evaporated with hydrochloric acid nearly to dryness. The residue was dissolved in water, and the barium sulfate was precipitated in the usual manner. The precipitate was washed with water, then with alcohol, and the suspension of the precipitate in alcohol transferred to a small collapsible steel beaker. The alcohol was evaporated under an infrared lamp, and the sulfate precipitate was uniformly deposited on an aluminum disc. The discs with precipitate were measured on a block counter. The results of the measurements are given in Tables 1 and 2. The data indicate that exchange is completely absent at the indicated temperature and time of exchange.

TABLE 2

Isotopic Exchange of Sulfur Between Sodium Hydrosulfide and Dimercaptopropanol at 37° (S^{35} contained in the dimercaptopropanol; mixture consisted of 320 mg NaHS and 1.065 g dimercaptopropanol in 100 ml of 80% alcohol)

Time of exchange (in hrs)	Activity of the hydrosulfide in the test sample without a ground (impulses/min)	Absolute static measurement error (impulses/min)
0	32	3
0.5	29	3
1	32	3
2	30	3
3.5	27	3
6.0	29	3
8.5	31	3
11	32	3
14	32	3

SUMMARY

A method for the synthesis of dimercaptopropanol, containing radioactive sulfur, was proposed. The method permits obtaining a compound with high activity. Running the reaction at room temperature facilitates the isolation of a pure substance.

It was shown that the exchange of sulfur between dimercaptopropanol and sodium hydrosulfide does not go at 37° in alcohol medium.

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STUDY OF THE CONDITIONS AND MECHANISM FOR THE SYNTHESIS OF PHOSPHORYLCHOLINE, CONTAINING P^{32}

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The preparation of intermediate metabolism products, containing labeled atoms, is of both great theoretical and practical interest. In the present study we investigated the conditions and mechanism for the synthesis of phosphorylcholine, containing P^{32} – the most important component of the lecithin molecule.

Methods have been described in the literature for the preparation of phosphorylcholine by the reaction of choline chloride with phosphorus oxychloride [1], from trimethylamine with chloroethyl phosphate, ethylene chlorohydrin and ethyl metaphosphate [2], and by the reaction of choline chloride with anhydrous orthophosphoric acid in the presence of phosphorus pentoxide [3-5] and without it [6]. In particular, the last method gave labeled phosphorylcholine for the first time with a 62% yield.

The method chosen by us for the preparation of phosphorylcholine was based on the reaction between choline chloride and anhydrous orthophosphoric acid in the presence of phorphorus pentoxide, since it gave the highest yield (78%). It was not indicated in the literature that it is necessary to operate in vacuo or that secondary synthesis products are formed, even though only traces of free choline remained after reaction [5]. The role played by the phosphorus pentoxide was also not clear, whether it functions as an esterification agent or whether it combines with the water liberated during reaction.

EXPERIMENTAL

To obtain a solution of orthophosphoric acid we took radioactive red phosphorus and burned it in the quartz tube of the apparatus shown in the figure, after which the obtained phosphorus pentoxide was dissolved in water. The solution was boiled for about an hour to convert any metaphosphoric acid, possibly formed in the dissolving of the phosphorus pentoxide in water, into orthophosphoric acid. The acid was dehydrated by the method described in the literature [7].

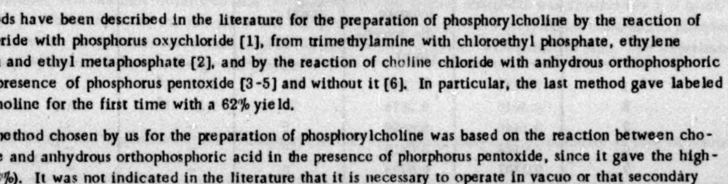

Diagram of the apparatus: 1) trap with $CaCl_2$; 2) trap with KOH; 4) reaction tube; 3,5,6) traps, cooled with a mixture of dry ice and acetone; 7) flasks with water.

Some preliminary experiments made to determine the optimum conditions for the synthesis of phosphorylcholine revealed that the reaction should be run at a temperature of 100° and a pressure of 1-2 mm: under these conditions it proceeds quantitatively. A complete dehydration of the acid is not observed at a lower vacuum and temperature, and the yield drops. Raising the temperature above 100° results in partial formation of the pyro form of the acid and of the ester. The use of powdered calcium oxide to remove the excess acid, based on the Plimmer method [1], led to the formation of very bulky precipitate, adsorbing a substantial amount of phosphorylcholine. Consequently, we used a magnesia mixture for this purpose.

To 6.0979 g (0.062 mole) of orthophosphoric acid was added 2.3593 g (0.017 mole) of choline chloride and the mixture was heated at 100° and a pressure of 1-2 mm until the evolution of hydrogen chloride bubbles ceased, after which 4.4385 g (0.031 mole) of phosphorus pentoxide was added, and the mixture was heated under the same conditions for 30 hours. The obtained glassy mass was dissolved in 200 ml of water, the solution treated with ammonia until weakly alkaline, and then boiled for about an hour. The excess phosphate ion was precipitated with magnesia mixture. Only traces of free choline (the reaction with Reinecke salt was frequently negative) were found to be present in the solution after the precipitation. We were satisfied that dicholine phosphate as impurity was absent due to the complete precipitation of the phosphate ion, which had been added in stoichiometric amount, calculated on the basis of 100% formation of phosphorylcholine.

TABLE 1

Activity of Successively Removed Calcium Chloride Precipitates from Phosphorylcholine Solution

Precipitate Nos.	Weight of precipitate (in g)	Weight of sample taken to measure the activity (in g)	Activity of the sample (impulses/ /min)	Specific activity (impulses/min)	Static error (in %)
1	2.5154	0.1908	271	$5.66 \cdot 10^3$	2
2	3.4210	0.2618	99	$1.57 \cdot 10^3$	3.3
3	0.1440	0.0563	0	–	–
4	0.0448	0.0215	0	–	–
5	0.3707	0.0798	0	–	–

To isolate the calcium salt of the ester, the solution, evaporated to a volume of 30-40 ml, was treated with an equivalent amount of calcium chloride, the solution evaporated to a volume of 10 ml, and then treated with 30 ml of alcohol. The obtained precipitate was filtered. The operation of evaporation and precipitation of the calcium salt with alcohol was repeated several times. The filtrate from the last filtration was evaporated to dryness, and the obtained precipitates were analyzed for their content of radioactive phosphorus (Table 1).

The obtained data show that all of the ester was isolated as the calcium salt after 2 precipitations of the evaporated solution with alcohol. The remaining precipitates represented ammonium chloride. The test with Nessler reagent revealed that ammonium chloride was present as impurity in the first precipitate. As can be seen from the data in Table 1, the second precipitate contained a substantial amount of ammonium chloride as impurity. The calcium salt of the ester is insoluble in alcohol, so that hot alcohol can be used to remove the last traces of ammonium chloride from it.

To elucidate the mechanism of choline esterification we synthesized phosphorylcholine, proceeding from radioactive orthophosphoric acid (Expts. 1 and 2, Table 2) and inactive phosphorus pentoxide, and also from radioactive phosphorus pentoxide and inactive orthophosphoric acid (Expt. 3, Table 2). The reaction course was determined by measuring the specific activity of the phosphorus of either the starting acid or phosphorus pentoxide, of the ester, and of the phosphate ion remaining after reaction.

The measurement results, presented in Table 2, show that both the orthophosphoric acid and the phosphorus pentoxide participate in the formation of the ester. The specific activity of the ester phosphorus was not an average value, which testified to the absence of equal distribution of the activity between the acid and its anhydride, on the one hand, and between the acid and its ester, on the other. In Expt. 2, where a higher vacuum (0.1-0.3 mm) was used, the fraction of the activity, going from the acid to the ester, increased to 79%. This result could also be interpreted as being due to possible exchange between the phosphate group of the ester and the phosphate ion, both in the reaction mixture and in the subsequent boiling. To verify the validity of such a postulation we ran some experiments on the exchange of phosphorylcholine with the phosphate at 100° in both neutral and acid media (2 N HCl). For this, weighed samples of recrystallized calcium salt of phosphorylcholine and of

TABLE 2

Fraction of Phosphoric Acid and of Phosphoric Anhydride Participating in the Formation of the Choline Ester

Expt. Nos.	Specific activity of the phosphorus (impulses/min)			Ratio of the specific activity of the ester and of the starting compound (in %)	Static error (in %)
	in the starting compound	in the ester	averaged		
1	$1.2 \cdot 10^5$	$6.8 \cdot 10^4$	$5.7 \cdot 10^4$	56.7	3.4
2	$1.06 \cdot 10^3$	$8.41 \cdot 10^2$	$3.8 \cdot 10^2$	79	4
3	$1.17 \cdot 10^5$	$6.1 \cdot 10^4$	$4.3 \cdot 10^4$	51.1	2

monosubstituted sodium phosphate, containing P^{32}, were dissolved in water. The solution, transferred to a 50-ml volumetric flask, was made up to the mark and then poured into a flask, fitted with a reflux condenser. Before heating the solution a sample (1 ml) was removed to determine the original activity of the phosphate ion. After this the solution was boiled, and at definite time intervals duplicate samples (1 ml) were removed with a pipette to determine the activity of the ester and of phosphate ion. The study of exchange in acid medium was run in a similar manner with the only difference that the monosubstituted sodium phosphate was dissolved in 2 N hydrochloric acid. The activity of the phosphate ion was determined in the form of magnesium ammonium phosphate, while the activity of the ester was determined in the form of the compound with Reinecke salt. The experimental data (Table 3) revealed that exchange was absent.

TABLE 3

Isotopic Exchange of Phosphorus Between Phosphorylcholine and Sodium Dihydrogen Phosphate at 100° in Neutral and Acid Media

Time of exchange (in hours)	Activity of phosphate ion (impulses/min)	Activity of the ester reineckate (impulses/min)	Absolute measurement error (impulses/min)	Time of exchange (in hours)	Activity of phosphate ion (impulses/min)	Activity of the ester reineckate (impulses/min)	Absolute measurement error (impulses/min)
In neutral medium				In acid medium			
0	6080	4	78	0	2560	1	51
1	6015	2	77	1	2560	0	51
2	5942	1	76	2	2516	5	50
3	5975	10	76	3	2510	10	50
5	5945	5	76	5	2526	3	50
7	6045	6	77	7	2546	0	51

SUMMARY

Choline is esterified quantitatively to phosphorylcholine under the conditions found by us. Both orthophosphoric acid and phosphorus pentoxide can be used as esterifying agents here.

At a pressure of 1-2 mm both of these phosphorylating agents participate to approximately the same extent in the formation of the ester bond. A reduction in the pressure increases the degree of acid participation in the reaction.

The stability of the ester bond is indicated by the absence of exchange between phosphorylcholine and monosubstituted sodium phosphate in both neutral and acid media at 100°.

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SYNTHESIS AND PROPERTIES OF TRISUBSTITUTED α-NAPHTHYLSILANE DERIVATIVES

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Organosilicon compounds, containing the naphthyl radical, have been inadequately studied. Several naphthyl-containing silicohydrocarbons have been described in the studies of A.D. Petrov and coworkers [1-5] and of Gilman and coworkers [6]; all of them were synthesized with the aid of magnesium or lithium from

$$\alpha\text{-}C_{10}H_7Si(OC_2H_5)_3,$$

with the exception of α-naphthyltrimethylsilane, whose attempted preparation by organomagnesium synthesis proved unsuccessful [7]. This apparently was due to steric hindrance, created by the naphthyl radical. The use of excess RMgX in the present study permitted us to surmount this difficulty and obtain α-$C_{10}H_7Si(CH_3)_3$, and also α-$C_{10}H_7Si(C_2H_5)_3$, in 70% yield.

To expand the possibilities of studying trisubstituted α-naphthylsilane derivatives we undertook the problem of improving the method for the preparation of α-$C_{10}H_7SiCl_3$, which up to now has not been used in the synthesis of organosilicon compounds; this is obviously due to the low yield (15-20%) and inadequate purity (a liquid with a boiling point range of 5°) of the α-$C_{10}H_7SiCl_3$, obtained by the Melzer method [8]. We were able to develop conditions for the preparation of pure α-naphthyltrichlorosilane (m.p. 53°) in 60% yield.

In studying the reaction of α-$C_{10}H_7SiCl_3$ with RMgX it was established that despite the greater mobility, when compared to the OC_2H_5 group, of chlorine atoms, the replacement of the latter by radicals occurs only at 80-100°; in this connection a uniform reduction in the reactivity of RMgX with increase in the molecular weight of the radical was observed; a similar rule also holds in the reaction of α-$C_{10}H_7SiCl_3$ with alcohols.

Besides α-naphthyltrialkoxysilanes, we also synthesized phenyltriallyloxysilane from $C_6H_5SiCl_3$ and allyl alcohol, despite the statement [9] that it is impossible to obtain the compound by this reaction.

EXPERIMENTAL

α-Naphthyltrichlorosilane. To the α-$C_{10}H_7MgBr$, prepared from 5.5 g of Mg, 36.4 g of α-$C_{10}H_7Br$ and 75 ml of ether, was added 38 g of $SiCl_4$. The next day the reaction mixture was heated on the water bath for 0.5 hour, after which a 1.5-fold excess of C_2H_5MgBr was added to the reaction flask, the flask contents heated at ether boil for another 2 hours, and then after distilling off the ether, for another 2 hours on a boiling water bath. After the usual operations we obtained by distillation:

tetraethylsilane, 8.5 g (30%), b.p. 150-152°, d_4^{20} 0.7652; α-naphthyltriethylsilane, 14.5 g,* b.p. 142-143° at 3 mm, and di-α-naphthyldiethylsilane, 3.5 g, b.p. 231-232° at 2 mm, d_4^{20} 1.1100.

Found %: C 84.05; H 6.78. $C_{24}H_{24}Si$. Calculated %: C 84.60; H 7.11.

b) α-$C_{10}H_7SiCl_3$ was prepared from 90 g (3.75 atoms) of Mg, 624 g (3 moles) of α-$C_{10}H_7Br$, 765 g (4.5 moles) of $SiCl_4$ and 2250 ml of ether. After adding the $SiCl_4$ the reaction mixture was stirred at 15-18° 10 days. The magnesium salts were removed by filtration, the ether and $SiCl_4$ were removed by distillation, and the residue was distilled to give 476 g (60%) of a fraction with b.p. 134-135° at 3 mm, which crystallized the next day; m.p. 53° (in a sealed capillary).

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*Corresponds to 15.6 g of α-$C_{10}H_7SiCl_3$.

Found %: C 46.25; H 2.85; Si 10.46; Cl 40.50. $C_{10}H_7SiCl_3$. Calculated %: C 45.90; H 2.70; Si 10.74; Cl 40.66.

α-Naphthyltrialkylsilanes from α-$C_{10}H_7Si(OC_2H_5)_3$

α-Naphthyltrimethylsilane. To the CH_3MgI, obtained from 85.2 g (0.6 mole) of CH_3I and 14.4 g (0.6 atom) of Mg, was added 14.5 g (0.05 mole) of α-$C_{10}H_7Si(OC_2H_5)_3$; after heating for 30 minutes on the water bath the ethyl ether was distilled off and replaced by isoamyl ether, in which the reaction mixture was heated for 4 hours at 140-150° (thermometer in the flask); the flask contents after cooling were decomposed with water and dilute sulfuric acid, and then extracted with ether. Removal of the ethers (ethyl and isoamyl) by distillation gave 7 g (70%) of α-naphthyltrimethylsilane with b.p. 102-103° at 2.5 mm; d_4^{20} 0.9821, n_D^{20} 1.5800.

α-Naphthyltriethylsilane was obtained under the same conditions by heating 0.05 mole of α-$C_{10}H_7Si(OC_2H_5)_3$ with a 4-fold amount of C_2H_5MgBr; here a liquid was obtained with b.p. 132-140° at 2.5 mm, which was again treated with excess C_2H_5MgBr at 140-150°; after the usual operations the α-naphthyltriethylsilane was isolated by distillation, b.p. 142-143° at 3 mm, d_4^{20} 0.9812, n_D^{20} 1.5728.

α-Naphthyltrialkylsilanes from α-$C_{10}H_7SiCl_3$

α-Naphthyltrimethylsilane. To the CH_3MgI, obtained from 4.3 g (0.18 atom) of Mg, 25.5 g (0.18 mole) of CH_3I and 100 ml of ether, was added 13 g (0.05 mole) of α-$C_{10}H_7SiCl_3$. After heating for 2 hours at ether boil the latter was distilled off, while the residue was heated on a boiling water bath for 1.5 hours. The earlier distilled ether was returned to the reaction flask, and the reaction product was treated with water and dilute sulfuric acid. After drying over Na_2SO_4 the ether layer was distilled and the fraction with b.p. 102-103° at 2.5 mm was collected (80% yield).

TABLE 1*

Compound	Boiling point (mm)	d_4^{20}	n_D^{20}	Empirical formula	MR_D calculated	MR_D found	Literature
α-Naphthyltrimethylsilane	102° (2.5)	0.9832	1.5809	$C_{13}H_{16}Si$	66.89	67.89	[3, 6]
α-Naphthyltriethylsilane	132 (2.5)	0.9804	1.5748	$C_{16}H_{22}Si$	80.84	81.69	
α-Naphthyltri-n-propylsilane	164 (4)	0.9533	1.5568	$C_{19}H_{28}Si$	94.78	96.04	[4]
α-Naphthyltri-n-butylsilane	183 (3)	0.9368	1.5432	$C_{22}H_{34}Si$	108.73	109.92	[1]
α-Naphthyltriallylsilane	151 (3)	0.9956	1.5938	$C_{19}H_{22}Si$	93.85	94.88	[5]

*Determination of the density and measurement of the refractive indices here and in Table 2 were done by T.V. Vystavkina.

Under similar conditions, but with different amounts of starting materials (C_2H_7Br and C_4H_9Br), we obtained: α-naphthyltriethylsilane in 82% yield from 39 g (0.15 mole) of α-$C_{10}H_7SiCl_3$, 58.9 g (0.54 mole) of C_2H_5Br and 12.9 g (0.54 atom) of magnesium.

Found %: C 79.37; H 9.34; Si 11.42. $C_{16}H_{22}Si$. Calculated %: C 79.26; H 9.15; Si 11.59.

α-Naphthyltri-n-propylsilane in 70% yield from 26.1 (0.1 mole) of α-$C_{10}H_7SiCl_3$, 55.4 g (0.45 mole) of

TABLE 2

Compound	Experiment temperature	Boiling point (mm)	d_4^{20}	n_D^{20}	MR_D		Found (%)			Empirical formula	Calculated (%)			Yield (in %)
					found	calculated	C	H	Si*		C	H	Si	
α-Naphthyltrimethoxysilane	—35°	139—140° (3.5)	—	—	—	—	63.07	6.52	11.11	$C_{13}H_{16}SiO_3$	62.91	6.45	11.31	84.5
α-Naphthyltriethoxysilane	—30	142—143 (3)	1.0580	1.5298	84.70	83.30	66.32	7.72	9.57	$C_{16}H_{22}SiO_3$	66.16	7.64	9.67	82.3
α-Naphthyltri-sec-propoxysilane	—25	156—158 (3)	1.0090	1.5120	98.65	97.24	68.68	8.48	8.61	$C_{19}H_{28}SiO_3$	68.63	8.49	8.45	81.6
α-Naphthyltri-n-butoxysilane	— 5	186—187 (3)	0.9967	1.5106	112.52	111.19	70.37	9.21	7.60	$C_{22}H_{34}SiO_3$	70.54	9.15	7.50	82.8
α-Naphthyltri-n-hexyloxysilane	15	212—213 (3)	0.9660	1.5018	140.10	139.08	73.32	10.19	6.31	$C_{28}H_{46}SiO_3$	73.30	10.11	6.13	80.8
α-Naphthyltri-(2-ethylhexyloxy)-silane	15	246—247 (3)	0.9482	1.4990	168.11	166.96	75.13	10.80	5.33	$C_{34}H_{58}SiO_3$	75.22	10.77	5.17	80.0
α-Naphthyltri-sec-oxtyloxysilane	15	235—236 (3)	0.9425	1.4945	167.84	166.96	75.00	10.85	5.26	$C_{34}H_{58}SiO_3$	75.22	10.77	5.17	81.0
α-Naphthyltricyclohexyloxysilane	20	242—243 (3)	1.0700	1.5440	133.56	132.24	74.20	8.97	6.30	$C_{28}H_{40}SiO_3$	74.30	8.90	6.20	80.0
α-Naphthyltriallyloxysilane	—32	169—170 (3.5)	1.0684	1.5460	95.81	96.75	69.90	6.86	8.72	$C_{19}H_{22}SiO_3$	69.90	6.79	8.61	80.0
Phenyltriallyloxysilane	—35	115—116 (3)	1.0142	1.4892	78.70	78.94	—	—	10.24	$C_{15}H_{20}SiO_3$	—	—	10.17	80.0

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* The silicon analyses were run by T.V. Vystavkina.

n-C_3H_7Br and 10.8 g (0.45 atom) of magnesium.

α-Naphthyltri-n-butylsilane in 76.5% yield from 26.1 g (0.1 mole) of α-$C_{10}H_7SiCl_3$, 123.3 g (0.9 mole) n-C_4H_9Br and 21.6 g (0.9 atom) magnesium.

α-Naphthyltriallylsilane. To 10.8 g (0.45 atom) of Mg and 50 ml of ether, contained in a flask, fitted with stirrer, condenser and dropping funnel, was added with vigorous stirring in 2 hours a solution of 13 g (0.05 mole) of α-$C_{10}H_7SiCl_3$ and 43.5 g of C_3H_5Br (0.36 mole) in 100 ml of ether. At the end of addition the reaction mixture was heated on the water bath for 30 minutes, after which it was treated with water and 25% NH_4Cl. The ether layer was dried over Na_2SO_4 and then distilled; the fraction with b.p. 151-152° at 3 mm weighed 11.5 g, which represents an 82.6% yield. The properties of the obtained silicohydrocarbons are listed in Table 1.

α-Naphthyltrialkoxysilanes. α-Naphthyltrimethoxysilane. A solution of 26.1 g (0.1 mole) of α-$C_{10}H_7SiCl_3$ and 23.7 g (0.3 mole) of pyridine in 40 ml of ether was charged into a 500-ml flask, fitted with condenser, stirrer, thermometer and dropping funnel. The reaction mixture was cooled to −35° and then from the dropping funnel in 1 hour, with vigorous stirring, was added methyl alcohol (0.4 mole), diluted with an equal volume of ether. The reaction was exothermic and proceeded with the precipitation of pyridine hydrochloride. After all of the alcohol had been added the cooling was discontinued, and the reaction mixture was stirred until it reached room temperature. Then the flask was heated on the water bath for 15 minutes; water was added to the cooled reaction mixture to dissolve the pyridine salt; the ether layer was separated from the water layer, which was extracted with 50 ml of ether; the combined ether extracts were dried over Na_2SO_4. After distilling off the ether the residue (23 g) was distilled at 3.5 mm to give 21 g (84.5%) of a liquid with b.p. 139-140°; the liquid crystallized after standing for 2 days; after recrystallization from alcohol the substance had m.p. 28°.

The other α-naphthyltrialkoxysilanes were obtained in a similar manner, the only change being variation in the experimental temperature used for each alcohol. The properties of the synthesized alkoxysilanes are listed in Table 2.

The molecular refraction for all of the synthesized compounds was calculated from the data of [10], in which connection a correction [11] was made for the allyl radical.

SUMMARY

1. Pure α-naphthyltrichlorosilane was synthesized for the first time.

2. Eight new α-naphthyltrialkoxysilanes were synthesized, and also the new phenyltriallyloxysilane and α-naphthyltriethylsilane.

3. It was shown that it is possible to obtain α-naphthyltrimethylsilane and α-naphthyltriethylsilane from α-$C_{10}H_7Si(OC_2H_5)_3$.

4. It was shown that different monoatomic alcohols react differently with α-naphthyltrichlorosilane.

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SYNTHESIS OF SOME FLUORINE-CONTAINING β-ARYL-β-ALANINES

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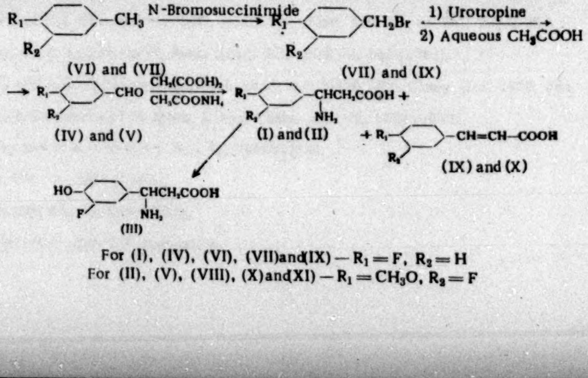
It is known that replacement of a hydrogen atom in the benzene ring of phenylalanine by fluorine leads to the formation of compounds, in their physiological action appearing as phenylalanine antagonists [1]. The question of a change in the properties of β-amino acids with a similar replacement has not been studied up to now; for this reason it seemed of interest to us to synthesize some fluorine-containing β-amino acids. In addition, another objective in the present investigation was to study the behavior of fluorine-containing aromatic aldehydes in the V.M. Rodionov reaction [2], being one of the better methods for the preparation of β-amino acids.

In the present study we synthesized two fluorine-containing β-amino acids: β-(p-fluorophenyl)-β-alanine (I) and β-(3-fluoro-4-methoxyphenyl)-β-alanine (II). The latter was then converted into β-(3-fluoro-4-hydroxyphenyl)-β-alanine [3-fluoro-β-tyrosine] (III) in connection with the fact that 3-fluorotyrosine proved to be an antagonist of the natural amino acid, tyrosine [3].

As is known, aldehydes are used as starting substances for the preparation of β-amino acids by the Rodionov method. To synthesize the above-mentioned fluorine-containing β-amino acids it was necessary to have p-fluorobenzaldehyde (IV) and 3-fluoro-4-methoxybenzaldehyde (V). Both of these aldehydes had been prepared before: p-fluorobenzaldehyde had been obtained from p-fluorotoluene by its oxidation with chromyl chloride in carbon bisulfide solution [4], and also through p-fluorobenzal bromide [5]; 3-fluoro-4-methoxybenzaldehyde had been obtained by the reduction of the corresponding nitrile [6]. However, these methods are inconvenient, and consequently we used the Sommelet method [7], which permits obtaining under mild conditions and very simply a conversion of the group CH_2X (where X is either halogen or the NH_2 group) into the aldehyde group, to obtain the aldehydes.

We obtained p-fluorobenzyl bromide from p-fluorotoluene (VI) by bromination of the latter with N-bromosuccinimide. The quaternary salt from p-fluorobenzyl bromide (VII) and hexamethylenetetramine (urotropine) when heated with dilute acetic acid gave p-fluorobenzaldehyde in 72% yield. 3-Fluoro-4-methoxybenzaldehyde was obtained in a similar manner from 3-fluoro-4-methoxytoluene (VIII).

Since it is indicated in the literature that in the synthesis of β-aryl-β-amino acids higher yields are obtained if the aldehyde is reacted with malonic acid in the presence of alcoholic ammonium acetate solution [8], then in the future we used this method. β-(p-Fluorophenyl)-β-alanine was obtained in 63% yield, in which connection we also isolated p-fluorocinnamic acid (IX) in 15% yield from the reaction mixture. β-(3-Fluoro-4-methoxyphenyl)-β-alanine was obtained by the Rodionov method in 58% yield; here the previously unknown 3-fluoro-4-methoxycinnamic acid (X) was isolated from the reaction mixture in 21.7% yield.



For (I), (IV), (VI), (VII) and (IX) — $R_1 = F$, $R_2 = H$
For (II), (V), (VIII), (X) and (XI) — $R_1 = CH_3O$, $R_2 = F$

To obtain 3-fluoro-β-tyrosine from β-(3-fluoro-4-methoxyphenyl)-β-alanine the latter was demethylated by heating with hydrobromic acid, followed by treatment of the formed hydrobromide with sodium acetate to give the free amino acid. The β-(p-fluorophenyl)-β-alanine and 3-fluoro-β-tyrosine were characterized as their benzoyl derivatives.

Physiological testing of the compounds, done at the All-Union Scientific-Research Chemical-Pharmaceutical Institute, revealed that the synthesized fluorine-containing β-amino acids do not possess the physiological action of the corresponding α-amino acids.

EXPERIMENTAL

p-Fluorotoluene and 3-fluoro-4-methoxytoluene were obtained from p-toluidine and cresidine, respectively, through the diazonium borofluorides by known methods [9].

p-Fluorobenzaldehyde (IV). a) p-Fluorobenzyl bromide (VII). A mixture of 15 g of p-fluorotoluene, 2.49 g of N-bromosuccinimide, 0.9 g of benzoyl peroxide and 100 ml of carbon tetrachloride was boiled for 2 hours. The succinimide was filtered, the solvent distilled from the filtrate, and the p-fluorobenzyl bromide isolated from the residue; yield 20 g (78%), b.p. 82° (10 mm); from [10]: b.p. 85° (15 mm).

b) Quaternary salt. A solution of 14 g of p-fluorobenzyl bromide and 10.1 g of urotropine in 120 ml of chloroform was boiled for 1 hour. After cooling, the precipitate of quaternary salt was separated; yield 22 g (92%).

c) Aldehyde. A mixture of 22 g of the quaternary salt and 100 ml of 50% acetic acid was boiled for 2 hours, then the mixture was poured into 200 ml of water, and the product was extracted with chloroform. The extracts were washed with sodium bicarbonate solution and then with water. Distillation gave p-fluorobenzaldehyde; yield 6 g (72%), b.p. 177-178°. From [4]: b.p. 174.5° (752 mm).

β-(p-Fluorophenyl)-β-alanine (I). A mixture of 6 g of p-fluorobenzaldehyde, 5.1 g of malonic acid, 7.7 g of ammonium acetate and 10 ml of alcohol was boiled on the water bath for 4.5 hours (a precipitate began to deposit after 1 hour). The precipitate of β-amino acid was separated, washed 3 times with hot alcohol, and dried in a vacuum-desiccator. Yield 5.6 g (63%), m.p. 223° (with decomposition, from water).

Found %: N 7.79, 7.89. $C_9H_{10}O_2NF$. Calculated %: N 7.65.

Dilution of the filtrate with water gave p-fluorocinnamic acid (IX); yield 1.2 g (15%), m.p. 206-207° (from alcohol). From [11]: m.p. 208°.

The β-amino acid was converted in the usual manner into N-benzoyl-β-(p-fluorophenyl)-β-alanine, m.p. 188-189° (from aqueous alcohol).

Found %: N 4.81, 4.96. $C_{16}H_{14}O_3NF$. Calculated %: N 4.88.

3-Fluoro-4-methoxybenzaldehyde (V). a) 3-Fluoro-4-methoxybenzyl bromide (XI). A solution of 40 g of 3-fluoro-4-methoxytoluene in 230 ml of carbon tetrachloride was simultaneously treated with 51 g of crushed N-bromosuccinimide and 0.6 g of benzoyl peroxide, and the mixture was boiled until the precipitate of N-bromosuccinimide disappeared. After cooling, the separated succinimide was filtered, the solvent was distilled from the filtrate, and the 3-fluoro-4-methoxybenzyl bromide isolated from the residue; yield 37.5 g (60%), b.p. 149-155° (28-25 mm). The product crystallized on standing: m.p. 39-41°. From [12]: m.p. 42°.

b) Quaternary salt. To a solution of 22.5 g of urotropine in 200 ml of chloroform was added 34 g of 3-fluoro-4-methoxybenzyl bromide and the mixture was heated on the water bath for 40 minutes. After cooling, the precipitate of quaternary salt was filtered and washed with chloroform; yield 50 g (90%).

c) Aldehyde. A solution of 43 g of the quaternary salt in 220 ml of 50% acetic acid was boiled for 1 hour. The solution was cooled, diluted with 250 ml of water, and the aldehyde extracted with chloroform. The extracts were washed with water, 1% soda solution, and again with water. The chloroform was distilled off, while the residue was vacuum-distilled in a stream of nitrogen. Yield of 3-fluoro-4-methoxybenzaldehyde 10 g (55%), b.p. 105-106° (5 mm), m.p. 28-30°. From [6]: b.p. 93° (3 mm), b.p. 29-30°.

β-(3-Fluoro-4-methoxyphenyl-β-alanine (II). A mixture of 5 g of 3-fluoro-4-methoxybenzaldehyde, 3.4 g of malonic acid, 6.8 g of ammonium acetate and 10 ml of alcohol was boiled on the water bath for 5 hours. The precipitate of amino acid was separated, washed with hot alcohol, and then with ether; yield 4 g (58%), m.p. 205-206°. After recrystallization from 30% alcohol, m.p. 211-212°.

Found %: N 6.30, 6.21. $C_{10}H_{12}O_3NF$. Calculated %: N 6.57.

The alcohol was distilled from the filtrate, and the residue was treated with water to separate the 3-fluoro-4-methoxycinnamic acid (X); yield 1.4 g (23%), m.p. 216-217° (from aqueous alcohol).

Found %: C 61.44, 61.18; H 4.83, 4.96. $C_{10}H_9O_3F$. Calculated %: C 61.22; H 4.59.

3-Fluoro-β-tyrosine (III). A solution of 3.8 g of β-(3-fluoro-4-methoxy)-β-alanine in 38 ml of hydrobromic acid was boiled for 2 hours. The warm solution was filtered; the filtrate on cooling deposited crystals of 3-fluoro-β-tyrosine hydrobromide, which were filtered, washed with alcohol, and then with ether. Weight 2 g. Evaporation of the filtrate in vacuo and shaking the residue with alcohol gave an additional 1.5 g of the hydrobromide. Total yield of hydrobromide 3.5 g (70%). A solution of 3.5 g of the hydrobromide in 5 ml of hot water was treated with a warm saturated solution of sodium acetate. The finely crystalline white precipitate obtained on cooling was filtered and washed with alcohol and ether. The yield of 3-fluoro-β-tyrosine was 1.9 g (78%), m.p. 163.5-164° (with decomposition, from water).

Found %: N 6.27, 6.28. $C_9H_{10}O_3NF \cdot H_2O$. Calculated %: N 6.44.

A sample of the compound after drying in vacuo at 100° melted at 169° (with decomposition).

Found %: N 7.18, 7.10. $C_9H_{10}O_3NF$. Calculated %: N 7.04.

O,N-Dibenzoyl-3-fluoro-β-tyrosine was obtained by treating a solution of the amino acid in soda solution with benzoyl chloride under cooling. M.p. 190.5-191.5° (from alcohol).

Found %: N 3.62, 3.67. $C_{23}H_{18}O_5NF$. Calculated %: N 3.44.

The substance is insoluble in dilute hydrochloric acid and gives a negative test for phenolic hydroxyl.

SUMMARY

1. The Rodionov method was used to synthesize β-(p-fluorophenyl)-β-alanine and β-(3-fluoro-4-methoxyphenyl)-β-alanine, and the latter was converted into 3-fluoro-β-tyrosine.

2. p-Fluorobenzaldehyde and 3-fluoro-4-methoxybenzaldehyde, required for the synthesis of the above amino acids, were synthesized from the corresponding benzyl bromides by the Sommelet reaction.

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MODELS OF THE PROTEIN MICROSTRUCTURE

I. SYNTHESIS OF N-AMINOACYL DERIVATIVES OF PHENYLALANINE ANHYDRIDE

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Based on an analysis of a number of studies on the isolation of preformed diketopiperazines from proteins it follows that the amino acids, found most widely distributed in the structure of the diketopiperazines, include leucine, phenylalanine, valine, proline, glycine and alanine. The anhydrides, composed from the indicated amino acids, have been isolated on numerous occasions from proteins and continue to be discovered in various types of naturally occurring substances [1]. As a result, both an analysis of the structure of a series of natural compounds and data on the amount of diketopiperazines in various proteins dictate the necessity of conducting investigations, whose purpose is to obtain model compounds simultaneously containing both cyclic and linear peptide structures. Such operation with models is a necessary stage in studies of the many-sided protein molecule.

Of the known bond forms in diketopiperazines the N-aminoacyl type of bond has been adequately substantiated at the present time [2]. Some synthesis studies made by us confirm its structure, and several derivatives with this type of bond, discovered recently in proteins and natural substances, support its being native.

Up to now a study of the N-aminoacyl derivatives of diketopiperazines has been made with models based on glycine anhydride. However, it is known that this anhydride has not been found once under natural conditions. Having obtained definite results when we used this readily available anhydride to develop a method for the synthesis of N-aminoacyl derivatives, we undertook the task of verifying this on more complex anhydrides. Considering the amino acid composition of the anhydrides isolated from protein, we settled on phenylalanine anhydride. Even the very first data obtained by us in studying the N-aminoacyl derivatives of this anhydride reveal that it is also possible to synthesize amidines. The preparation of (N-aminoacyl)-phenylalanine anhydrides by our method proceeds much more easily than in the case of glycine anhydride. That these derivatives are labile follows from a study of their reaction products with hydrazine and with amino acids. The stability of the —NH—CO— bond in phenylalanine anhydride is disturbed by the introduction of the amino acid radical R—N—CO— into the anhydride.

In contrast to phenylalanine anhydride, failing to cleave even when heated with 20% NaOH, its N-aminoacyl derivatives give the biuret reaction, being decomposed with 4% NaOH in the cold.

EXPERIMENTAL

1. Phenylalanine anhydride. A mixture of 5 g of phenylalanine and 30 ml of glycol was heated for 2 hours at 170°. Complete solution was observed in 30 minutes. The precipitate obtained on cooling was filtered and washed with methyl alcohol. Yield 3.2 g (71%). M.p. 290-291° [3] (from acetic acid). Soluble in xylene and nitrobenzene when heated, and insoluble in water and the alcohols. The picric acid and biuret reactions were negative.

Found %: N 9.59, 9.69. $C_{18}H_{18}O_2N_2$. Calculated %: N 9.53.

2. Phthaloylvaline. To 12.65 g of phthalic anhydride, fused at 150°, was added 10 g of valine and the mixture heated for another 30 minutes at 150°. The melt was poured into a beaker and then treated with water. The obtained precipitate was filtered and washed with water. Yield 69%. M.p. 165°. According to [4]: m.p. 165-167°.

3. Phthaloylvalyl chloride. A mixture of 7.41 g of phthaloylvaline, 6.24 g of phosphorus pentachloride and 120 ml of dry benzene was heated at 60° for 30 minutes. The clear solution was concentrated in vacuo to a small volume and precipitated with petroleum ether. The precipitate was filtered. Yield 7.0 g (70%). M.p. 89°.

4. N,N'-Di(phthaloylvalyl)phenylalanine anhydride (I). A mixture of 4 g of phenylalanine, 7 g of phthaloylvalyl chloride and 100 ml of anhydrous xylene was heated for 2 hours at 140°. Complete solution was obtained in 30 minutes, and after heating for 2 hours the solution was concentrated in vacuo. The residue was dissolved in benzene, the benzene solution treated with water to remove traces of hydrochloric acid, then concentrated to half volume, and precipitated with petroleum ether. The obtained oil was separated by decantation from the solution, and when a new portion of petroleum ether was added it crystallized. Yield 6.5 g (63.5%). M.p. 120°. Not reported in the literature. When treated with 0.1 N alkali in alcohol (Willstätter titration conditions) the compound decomposed to phthaloyl tripeptide and phthaloylamino acid. The amount of alkali consumed for the titration corresponds to four carboxyl groups. The compound is soluble in ether, benzene, acetone, chloroform and the alcohols, and insoluble in water and in alkali.

Found %: C 70.07, 70.19; H 5.31, 5.29; N 7.48, 7.54. $C_{44}H_{40}O_8N_4$. Calculated %: C 70.19; H 5.36; N 7.44.

The following was done to prove the structure of compound (I).

a) Investigation of the amino acid composition. Fifty mg of the substance was hydrolyzed with 10% hydrochloric acid for 36 hours. Chromatographing on paper (solvent butanol-water-acetic acid) indicated the presence of two amino acids – valine and phenylalanine.

b) Proof of the presence of phenylalanine anhydride. A solution of 0.5 g of N,N'-di(phthaloylvalyl)phenylalanine anhydride in 5 ml of anhydrous alcohol was treated with 0.12 g of hydrazine hydrate. The solution on standing began to deposit crystals, which were filtered and then washed with alcohol and with ether. M.p. 301° [5]. Yield 0.19 g, i.e., the theoretical yield, based on phenylalanine anhydride.

Found %: C 73.35, 73.20; H 6.36, 6.48; N 9.71, 9.72. $C_{18}H_{18}O_2N_2$. Calculated %: C 73.43; H 6.17; N 9.53.

A precipitate was isolated from the alcohol filtrate, which was recrystallized from 50% alcohol. Under the microscope the crystals appeared as needles, collected in clusters. M.p. 360°. Only valine was revealed when the hydrolyzate of this substance was chromatographed on paper (solvent butanol-water-acetic acid). As a result, the reaction of N,N'-di(phthaloylvalyl)phenylalanine anhydride with hydrazine gave phenylalanine anhydride and phthaloylvalyl hydrazide. This confirms the validity of the structure of (I) and permits postulating the scheme for the decomposition of the compound when reacted with hydrazine.

A similar reaction with hydrazine hydrate was also run with the substance obtained in the decomposition of the copper complex from N,N'-di(phthaloylvalyl)phenylalanine anhydride. For this 0.5 g of the substance was treated with 5 ml of anhydrous alcohol and 0.12 g (4 moles) of hydrazine hydrate. A precipitate of phenylalanine anhydride was not formed even after standing for several days. The original compound was recovered unchanged, which indicates that both phenylalanine anhydride and a linear structure are absent in the isolated substance (II).

c) Investigation of the copper biuret complex. Preparation of a solution of the copper biuret complex. A solution of 3 g of N,N'-di(phthaloylvalyl)phenylalanine anhydride in 50 ml of 50% alcohol was treated with an equal volume of 4% alcoholic caustic solution, and then a 25% alcoholic solution of $CuCl_2$ was added in drops until the flocculent copper hydroxide precipitate remained permanent. The solution was shaken on a shaker for a day, and the $Cu(OH)_2$ was separated by centrifuging. The clear solution of the copper complex was diluted with 50% alcohol to a substance concentration of 0.4%. An SF-4 spectrophotometer was used for the spectrophotometric analysis of the solution. The absorption maximum proved to be at a wavelength of 550 mμ (see table).

Decomposition of the complex. A solution of the copper biuret complex was decomposed by acidification with 10% hydrochloric acid. The acid solution was extracted with benzene until the biuret test was negative (in the solution when made alkaline). The benzene extract, dried over $CaCl_2$, was concentrated in vacuo, without heating, to an oily residue, which crystallized on standing in a vacuum-desiccator. Yield 1.7 g. M.p. 155°.

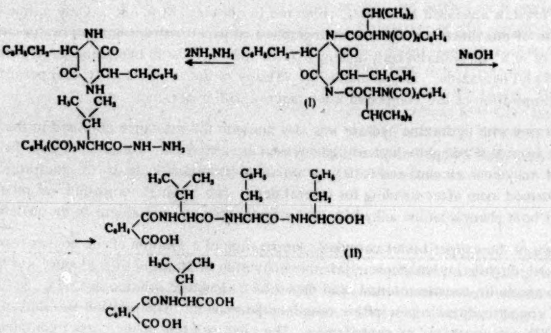
Spectrophotometric Data for Solutions of Copper Biuret Complexes

Wavelength λ (in mμ)	Optical density values ε			
	N,N'-di(phthaloylvalyl)phenylalanine anhydride	N-(phthaloylvalylphenylalanyl)phenylalanine	N,N'-di(phthaloylleucyl)phenylalanine anhydride	N-(phthaloylleucylphenylalanyl)-phenylalanine
500	0.736	0.501	0.538	0.582
510	0.812	0.541	0.586	0.606
520	0.860	0.578	0.623	0.678
530	0.896	0.601	0.646	0.714
540	0.918	0.618	0.648	0.724
550	0.926	0.642	0.650	0.728
560	0.908	0.631	0.635	0.708
570	0.874	0.605	0.605	0.670
580	0.816	0.552	0.566	0.590
590	0.774	0.453	0.511	0.528
600	0.648	0.399	0.461	0.508
610	0.556	0.351	0.405	0.454
620	0.484	0.306	0.343	0.398

Readily soluble in acetone and the alcohols. It gives the biuret reaction with absorption maximum at 550 mμ when run in alcohol. Chromatographing on paper revealed that two amino acids – valine and phenylalanine (II) – were present in this compound after its hydrolysis.

Found %: C 66.59, 66.67; H 5.76, 5.74; N 7.74, 7.76. $C_{31}H_{33}O_7N_3$. Calculated %: C 66.53; H 5.94; N 7.51.

Below we present the scheme for the decomposition of N,N'-di(phthaloylvalyl)phenylalanine anhydride (I) when reacted with hydrazine and when reacted with NaOH under the conditions of forming the copper biuret complex.



5. Phthaloylleucine. Ten grams of phthalic anhydride was melted in a glycerine bath, 9 g of leucine added to the melt, and the mixture heated for another 30 minutes at 150°. The obtained melt was dissolved in alcohol, filtered from unreacted leucine, concentrated, and precipitated with water. The oil obtained here crystallized on standing. Yield 76%. M.p. 115-117°. From [6]: m.p. 116°.

6. Phthaloylleucyl chloride. A mixture of 5 g of phthaloylleucine and 4 g of phosphorus pentachloride was heated in anhydrous benzene at 60° for 1 hour, at the end of which time solution was complete. The benzene solution was concentrated in vacuo, and the residue was precipitated with petroleum ether. Yield 83%. M.p. 60°. From [7]: m.p. 60°.

7. N,N'-Di(phthaloylleucyl)phenylalanine anhydride (III). A mixture of 3 g of phthaloylleucyl chloride and 1.2 g of phenylalanine anhydride in 60 ml of anhydrous xylene was heated for 1.5 hours at 140°. The substance was isolated in the same manner as described for the N,N'-di(phthaloylvalyl)phenylalanine anhydride. M.p. 89°. Yield 40%. Not reported in the literature. Soluble in ether, benzene, acetone, chloroform and the alcohols; insoluble in petroleum ether, in water and in alkali.

Found %: C 70.72, 70.53; H 6.14, 5.81; N 6.83, 6.95. $C_{46}H_{44}O_8N_4$. Calculated %: C 70.76; H 5.68; N 7.18.

To prove the structure of compound (III) we did the following: ran the chromatographing of the hydrolyzate on paper, reacted with hydrazine, and investigated the copper biuret complex.

a) Investigation of the amino acid composition. Fifty mg of the substance was hydrolyzed with 20% hydrochloric acid for 24 hours. After evaporation of the hydrolyzate and removal of the hydrochloric acid by repeated vacuum-distillation we ran a chromatographic analysis on paper. The solvent was butanol-water-acetic acid. Two amino acids were shown to be present: leucine and phenylalanine.

b) Proof of the presence of phenylalanine anhydride in the compound was shown by reaction with hydrazine hydrate. The quantitative amount of phenylalanine anhydride was isolated. M.p. 301°.

c) Investigation of the copper biuret complex. The copper biuret complex of N,N'-di(phthaloylleucyl)-phenylalanine anhydride was prepared in the same manner as described for the N,N'-di(phthaloylvalyl)phenylalanine anhydride. The absorption maximum of the solution was at 550 mμ (see table). Chloroform was used to extract the substance from the decomposed copper complex. The chloroform solution was dried over Na_2SO_4, concentrated to half volume, and precipitated with petroleum ether. M.p. 112°. Readily soluble in acetone and the alcohols. Gives the biuret reaction with absorption maximum at 550 mμ when run in alcohol. Chromatographing of the substance after hydrolysis on paper indicated the presence of the two amino acids leucine and phenylalanine in this compound.

As a result of studying the properties of the obtained phenylalanine anhydride derivatives we came to the conclusion that the acyl type of bond is exceedingly labile. This reactivity (lability) consists of: 1) the ease with which phenylalanine anhydride is acylated with amino acid chlorides, and 2) the removal of the whole aminoacyl radical when reacted with hydrazine.

SUMMARY

1. The synthesis of the N-aminoacyl derivatives of phenylalanine anhydride: N,N'-di(phthaloylvalyl)-phenylalanine anhydride and N,N'-di(phthaloylleucyl)phenylalanine anhydride, was described.

2. It was shown that when reacted with hydrazine these derivatives are decomposed at the N-aminoacyl bond. This was verified by the isolation of the hydrazides of N-phthaloylvaline and N-phthaloylleucine.

3. The behavior of these derivatives was studied under the conditions used to form copper biuret complexes. Reaction with 4% NaOH leads to cleavage of the phenylalanine anhydride contained in the compounds, which was shown by the isolation of N-phthaloylvalyl- and N-phthaloylleucyl-phenylalanylphenylalanines.

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SOME OF THE PROPERTIES OF N-BENZYLATED PEPTIDES. I

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When it had been shown that the peptide link in proteins was the commonest type of link between amino acids, the attention of scientists was turned to finding a method for successively connecting molecules of various amino acids using anhydride-type bonds. The development of a method for preparing this type of compound, peptides, was and is being directed primarily towards finding substituents for the amino group. Although Fischer [1] showed that it was possible to convert free amino acids into acid chlorides, as experimental material collected, it became clear that the amino group had to be protected by some method or other to eliminate side reactions during the preparation of acid chlorides. Thus, the development and perfection of methods for peptide synthesis required the correct choice of a protection for the amino group. In selecting it, the main interest was directed toward the development of methods which did not require the removal of an acetyl group by hydrolysis.

Carbobenzoxy protection of the amino group, proposed by Bergmann [2], played a large role in the synthesis of peptides. This method is now of paramount importance. The potentialities of this method were illustrated by its recent application to the synthesis of a pentapeptide [3] and oxytocin [4]. However, besides the obvious advantages of Bergmann's carbobenzoxy method in comparison with others (acetyl, benzoyl, chloro- and bromoacetyl, toluene- and benzenesulfonyl, phthalyl, etc.), it also has a series of disadvantages. Among them is the method of synthesis of carbobenzoxy chloride, using phosgene, and the use of its derivatives in peptide synthesis. Carbobenzoxyamino acid chlorides are very readily converted into Leuch's anhydrides [5] especially when heated. Similar formation of five-membered rings is observed in carbobenzoxypeptides in the form of esters. However, these disadvantages are easily eliminated in peptide synthesis, which requires a low temperature and thus prevents cyclization of the carbobenzoxyamino acid chlorides used. The latter cannot be used for preparing N-aminoacyldiketopiperazines due to their instability to heating, which is one of the necessary conditions for the aminoacylation of diketopiperazines.

Recently, attention has been paid to benzyl protection which was found to be as convenient and, in addition, superior in certain respects to the carbobenzoxy method [6]. In using this method for peptide synthesis, its experimental advantages were found to be: 1) the presence of a benzyl group facilitates the preparation of amino acid chlorides; the latter are readily separated from PCl_5, 2) derivatives of N-benzylated amino acids and dipeptides form hydrochlorides which crystallize well and are difficultly soluble in water; the latter considerably simplifies their isolation and identification, 3) the benzyl group of N-benzylamino acids and dipeptides is readily removed with hydrogen in glacial acetic acid in the presence of palladium black.

The methods of synthesizing N-benzyl derivatives of amino acids, given in the literature, are either direct treatment of α-halo derivatives of aliphatic acids with benzylamine [7] or direct treatment of amino acids or their esters with benzyl chloride of benzaldehyde [6]. Mono- and dibenzylated amino acids were obtained by these methods. The acid chloride method was used for synthesis of benzyldipeptides [6].

EXPERIMENTAL

I. Synthesis of N-Benzyldipeptides

N-benzyl-glycyl-phenylalanine. Chloroacetyl phenylalanine, synthesized by Fischer's method [8], was kept for 7 days with a five-fold amount of benzylamine. The excess benzylamine was removed with ether in an extractor with the addition of several drops of 4% NaOH. The aqueous solution was separated from the ethereal one and acidified with CH_3COOH. The precipitate was filtered off and washed with water. After recrystallization

TABLE 1

Spectrophotometric Data on Solutions of N-Benzyldipeptide Copper Biuret Complexes

Wavelength λ (in mμ)	Optical density values of 0.5% solutions of copper biuret complexes (ε)			Wavelength λ (in mμ)	Optical density values of 0.5% solutions of copper biuret complexes (ε)		
	N-benzyl-glycyl-phenyl-alanine	N-benzyl-alanyl-phenyl-alanine	N-benzyl-leucyl-valine		N-benzyl-glycyl-phenyl-alanine	N-benzyl-alanyl-phenyl-alanine	N-benzyl-leucyl-valine
500	0.315	0.262	0.300	590	0.939	0.805	0.750
510	0.351	0.296	0.314	600	0.985	0.845	0.777
520	0.418	0.357	0.361	610	1.025	0.881	0.788
530	0.474	0.406	0.402	620	1.035	0.895	0.800
540	0.541	0.462	0.452	630	1.000	0.861	0.755
550	0.610	0.521	0.509	640	0.952	0.819	0.706
560	0.692	0.591	0.537	650	0.863	0.748	0.648
570	0.781	0.645	0.640	660	0.771	0.663	0.575
580	0.858	0.731	0.692				

from water, the m.p. was 175°. The yield was 85%. The ninhydrin reaction was negative; the biuret reaction – positive. The absorption maximum lay at a wavelength of 620 mμ (Table 1). On heating with $CuCO_3$ it gave a copper salt.

Found %: C 69.13; H 6.56; N 8.78. $C_{18}H_{20}O_3N_2$. Calculated %: C 69.23; H 6.41; N 8.97.

The $C_6H_5CH_2NH$-groups in N-benzyl-glycyl-phenylalanine and the N-benzyldipeptides described below were determined by titration with 0.1 N NaOH in alcohol (Willstätter's method) and the results are given in Table 2.

N-Benzyl-alanyl-phenylalanine. α-Bromopropionyl phenylalanine [8] was kept for 5 days with a threefold amount of benzylamine. After adding 4% NaOH to the solution, the benzylamine was extracted with ether (in a separating funnel). When the ether had been removed by blowing through air, the solution was acidified with CH_3COOH. The precipitate was filtered off and washed with water until there was no reaction for halogen and then acetone. The m.p. was 235°. The yield was 75%. The ninhydrin reaction was negative. The biuret – positive (absorption maximum at 620 mμ). On heating with $CuCO_3$ it gave a copper salt.

Found %: C 69.78; H 6.68; N 8.38. $C_{19}H_{22}O_3N_2$. Calculated %: C 69.91; H 6.79; N 8.58.

TABLE 2

N-Benzylpeptide	Empirical formula	Nitrogen of $C_6H_5CH_2NH$-groups (in %)	
		calculated	found
N-Benzyl-glycyl-phenyl-alanine	$C_{18}H_{20}O_3N_2$	4.48	4.62
N-Benzyl-analyl-phenyl-alanine	$C_{19}H_{22}O_3N_2$	4.29	4.32
N-Benzyl-valyl-phenyl-alanine	$C_{21}H_{26}O_3N_2 \cdot HBr$	3.22	3.26
N-Benzyl-leucyl-phenyl-alanine	$C_{22}H_{28}O_3N_2$	3.80	3.76
N-Benzyl-leucyl-valine	$C_{18}H_{28}O_3N_2$	4.37	4.28

N-Benzyl-valyl-phenylalanine. Bromoisovaleryl phenylalanine was synthesized according to the data in [9]. 8 g of bromoisovaleryl phenylalanine, with m.p. 135°, was mixed with 15 ml of benzylamine and 25 ml of water. After standing for 2 weeks, the precipitate was filtered off and washed with water. The weight of the dry precipitate was 4 g. After recrystallization from hot water it had m.p. 168-169°. The yield was 60%. It was insoluble in water and acetone, but soluble in alcohol. It contained halogen. The picric acid and biuret reactions were negative, the ninhydrin – positive. Paper chromatographic analysis showed phenylalanine and N-benzyl-valine in the hydrolyzate and only one spot for the unhydrolyzed substance.

Found %: C 58.17, 58.20; H 6.22, 6.27; N 6.48, 6.59. $C_{21}H_{26}O_3N_2 \cdot HBr$. Calculated %: C 57.94; H 6.02; N 6.44.

N-Benzyl-leucyl-phenylalanine. Bromocaproyl phenylalanine was synthesized by the method described for bromoisocaproyl phenylalanine [10]. 7 ml of benzylamine and 3 ml of water were added to 2 g of bromocaproyl phenylalanine. On shaking for 15 minutes, everything dissolved. After 4 days the clear solution was made alkaline with 2 ml of 4% NaOH and extracted twice with ether (in a separating funnel). The aqueous solution was acidified with CH_3COOH. The precipitate was filtered off and washed with water and acetone. The m.p. was 139-140°. The yield was 59%. It was soluble in water on heating and also in alcohol. It did not contain halogen. The picric acid and biuret reactions were negative, the ninhydrin – positive. Paper chromatography of the hydrolyzate showed two amino acids – phenylalanine and N-benzylleucine.

Found %: C 71.81; H 7.86; N 7.47. $C_{22}H_{28}O_3N_2$. Calculated %: C 71.69; H 7.66; N 7.60.

N-Benzyl-leucyl-valine. Bromocaproyl valine was synthesized according to [11]. N-Benzyl-leucyl-valine was prepared from bromocaproyl valine and benzylamine in water. The benzylamine was used in a 5-fold excess. The mixture was kept for 7 days. The excess benzylamine was removed with ether in an extractor after ammonia had been added to the solution. The aqueous solution was separated and acidified with CH_3COOH. The precipitate was filtered off and washed with water, alcohol and acetone. To remove traces of halogen the precipitate was treated with ammonia, in which it dissolved, and as the NH_3 was removed in vacuum it again precipitated. The precipitate, treated in this way, was filtered off and washed with water and acetone. The m.p. was 196°. The yield was 75%. It was insoluble in water and acetone. It did not contain halogen. The ninhydrin reaction was negative, the biuret – positive (absorption maximum 620 mμ).

Found %: C 67.43; H 8.90; N 8.61. $C_{18}H_{28}O_3N_2$. Calculated %: C 67.48; H 8.81; N 8.74.

II. Synthesis of N-Benzyl Anhydrides of Amino Acids

N-Benzyl-(glycyl-phenylalanine) anhydride. N-Benzyl-glycyl-phenylalanine was heated to boiling in nitrobenzene; all the material dissolved. The solution was heated until water was no longer evolved (crepitation). On cooling, a precipitate formed, which was filtered off and washed with alcohol. The substance was recrystallized from water and dried at 100° over P_2O_5 (in a Fischer pistol) and had m.p. 175°. The yield was 85%. The biuret reaction was negative, the picric acid – positive on performing it in dioxane.

Found %: C 73.33, 73.32; H 6.22, 6.27; N 9.43, 9.62. $C_{18}H_{18}O_2N_2$. Calculated %: C 73.43; H 6.17; N 9.53.

N-Benzyl-(leucyl-valine) anhydride. 0.5 g of N-benzyl-leucyl-valine was heated in 5 ml of glycol on an oil bath for 1 hour. The clear solution was left to cool. The precipitate was filtered off and washed with water to remove the glycol. The substance was recrystallized from water and had m.p. 196°. The biuret reaction was negative, the picric acid reaction – positive. It was soluble in alcohols and acetone and insoluble in water and alkali.

Found %: C 71.41, 71.37; H 8.59, 8.61; N 9.13, 9.15. $C_{18}H_{26}O_2N_2$. Calculated %: C 71.50; H 8.67; N 9.27.

N-Benzyl-(leucyl-phenylalanine) anhydride. 0.5 g of N-benzyl-leucyl-phenylalanine was heated with 5 ml of nitrobenzene on a glycerine bath for 15 minutes, until water vapor was no longer evolved. The clear solution was left to cool to room temperature. The precipitate was filtered off and washed with acetone and ether. The m.p. was 137-139°. The yield was 60%. The biuret reaction was negative, the picric acid – positive. It was insoluble in alkali and acetone but soluble in alcohol.

Found %: C 73.37; H 7.29; N 7.86. $C_{22}H_{26}O_2N_2$. Calculated %: C 75.40; H 7.45; N 8.00.

SUMMARY

1. The following N-benzyl-dipeptides were synthesized: N-benzyl-glycyl-, N-benzyl-alanyl-, N-benzyl-valyl- and N-benzyl-leucyl-phenylalanines and N-benzyl-leucyl-valine.

2. N-Benzyl-(glycyl-phenylalanine), N-benzyl-(leucyl-phenylalanine) and N-benzyl-(leucyl-valine) anhydrides were synthesized.

3. N-Benzyldipeptides were prepared by treating the α-haloacylamino acid with benzylamine in an aqueous medium.

4. N-Benzyl anhydrides were prepared by cyclization of N-benzyl-dipeptides in nitrobenzene or glycol.

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INTRAMOLECULAR HYDROGEN BONDING AND ULTRAVIOLET ABSORPTION SPECTRA

V. THE INFLUENCE OF ACIDS ON THE ELECTRONIC SPECTRA OF AMINOACETOPHENONES

A.E. Lutsky and V.V. Dorofeev

The presence of acid neutralizes the optical effects of amino or imino groups. As a result,a spectrum is obtained corresponding to that of the compound without these groups. Thus, in the presence of HCl, aniline gives the spectrum of benzene, nitroaniline that of nitrobenzene [1] and diphenylamine that of diphenyl [2]. This is because the two unshared electrons of the nitrogen atom become involved in chemical bonds when the ammonium ion is formed, and can no longer interact with the π-electrons of the benzene ring.

Concentrated sulfuric acid affects not only the amino group, but also other functional groups, such as carbonyl. When ketones or other compounds containing carbonyl groups are dissolved in concentrated H_2SO_4, there is a shift in the absorption toward longer wavelength and weak bands appear in the long-wave region. In this case, the results have been interpreted [3, 5] by supposing that C=O behaves as a weakly basic group and that oxonium compounds are formed between the acid and solute.

To check the nature of the effect of acid on the electronic spectra of compounds whose molecules contain both the above-mentioned functional groups capable of reaction with acid, we have determined absorption curves for the isomeric aminoacetophenones and N-acetylamino- and N,N-dimethylamino-acetophenones, in aqueous HCl and H_2SO_4 of different strengths, and also in concentrated H_2SO_4.

Spectra in Aqueous HCl

In previous investigations of the absorption spectra of aminoacetophenone in aqueous HCl [6, 7],it was found that the effect of acid was most marked on the para and least on the meta isomer, and that all three isomers in HCl solution gave absorption spectra coinciding with that of unsubstituted acetophenone. In the present paper, a more detailed study has been made of the effect of HCl on the spectra of aminoacetophenones.

As may be seen from Figures 1 and 3-5, the use of 38.1% HCl instead of water as solvent produces a marked shift of the absorption spectra of all the isomeric aminoacetophenones toward shorter wavelength and the resulting spectra differ very little from each other or from that of unsubstituted acetophenone in water. However, they are not exactly the same as the acetophenone spectrum, since the latter contains an additional long-wave band with a maximum at 3325 A (ε 50). When the concentration of HCl is reduced to 13.6% this band begins to appear with all the isomers (Figure 2). At still greater dilution (0.7% HCl) the long-wave part of each spectrum is significantly displaced toward longer wavelengths, and its position approaches that in the spectrum in water (Figures 3-5). In the case of m-aminoacetophenone this displacement occurs at a higher dilution (0.07% HCl), which is evidence for the great stability of the hydrochloride of the meta isomer.

In contrast to the aminoacetophenones, the isomeric N-acetylaminoacetophenones in 38.1% HCl give absorption curves differing from that of unsubstituted acetophenone in water (Figure 6). The positions of the maxima of most of the bands remain almost the same as in neutral solution, but with o- and m-N-acetylaminoacetophenones there is a slight displacement of the long-wave band toward shorter wavelengths, and with the former there is a noticeable (four-fold) decrease in its intensity. In 13.6% HCl the absorption curves for all the isomers coincide with those of their solutions in neutral water (Table 1). Clearly, in contrast to the aminoacetophenones, the presence of HCl in solutions of the N-acetylaminoacetophenones does not eliminate the previously noted [9] special features of their spectra, which, in the case of the ortho isomer, afford evidence of intramolecular hydrogen bonding. N-Acetylaminoacetophenones, especially when dissolved in 13.6% HCl, do not form salts, and the tendency to salt formation is weakest in the case of the para isomer.

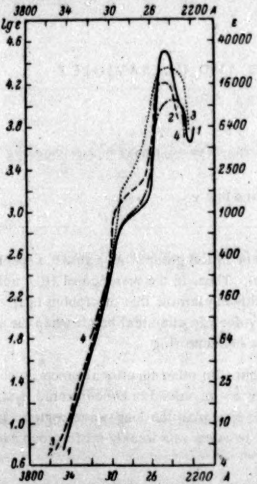

Fig. 1. Aminoacetophenones in 38.1% hydrochloric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) o-Aminoacetophenone (max. 2455 and 31700, inflection 2800 and 935, min. 2240 and 4470) (here the first number gives the wavelength in A and the second gives the value of ε); 2) m-aminoacetophenone (max. 2475 and 16300, inflection 2820 and 1556); 3) p-aminoacetophenone (max. 2405 and 22400, inflection 2830 and 2000); 4) acetophenone in water [8] (10^{-2}-10^{-5} M) (max. 3325 and 50, 2495 and 11000, inflection 2800 and 1150).

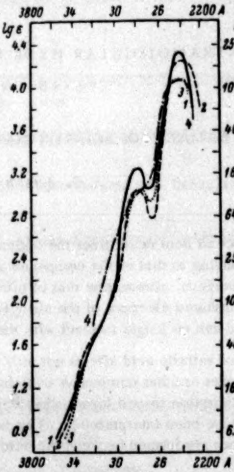

Fig. 2. Aminoacetophenone in 13.6% hydrochloric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) o-Aminoacetophenone (inflection 3115 and 100, max. 2800 and 1590, 2400 and 20500, min. 2705 and 1200); 2) m-aminoacetophenone (inflection 3030 and 120, max. 2815 and 1050, 2835 and 17000, min. 2695 and 590); 3) p-aminoacetophenone (inflection 3030 and 120, max. 2785 and 1080, 2415 and 10800, min. 2695 and 870); 4) acetophenone in water [8].

In the presence of HCl the N,N-dimethylaminoacetophenones (Figure 7 and Table 2) behave exactly like the aminoacetophenones.

Spectra in Concentrated and Aqueous H_2SO_4

As shown in Figure 8, o-aminoacetophenone gives the same two absorption bands in 99.8% H_2SO_4 as in aqueous solution. However, the long waveband only persists in the form of an inflection, considerably displaced toward shorter wavelength (the max. is shifted to 320 A) and reduced to about one-fifth of its intensity, resembling that of acetophenone in aqueous solution. The short waveband is displaced towards longer wavelength. It is otherwise with m- and p-aminoacetophenones. Their absorption curves in concentrated H_2SO_4 are quite different to those in water, as they show high intensity bands in the middle region of the ultraviolet. Their short wavebands are absent in H_2SO_4. Absorption curves at a number of bands and near to the bands of unsubstituted acetophenone

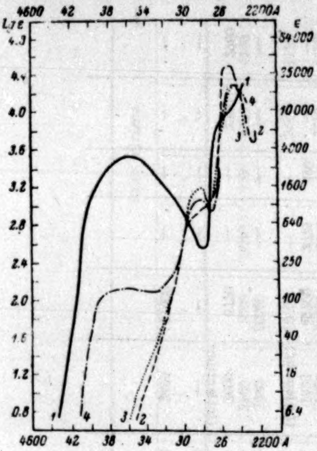

Fig. 3. o-Aminoacetophenone in different solvents. 1) In water ($2 \cdot 10^{-2}$-$2 \cdot 10^{-5}$ M) (max. 3580 and 3550, inflection 2580 and 7780, min. 2770 and 370); 2) in 38.1% hydrochloric acid; 3) in 13.6% hydrochloric acid; 4) in 0.7% hydrochloric acid ($2 \cdot 10^{-2}$-$2 \cdot 10^{-5}$ M) (inflection 3525 and 115, max. 2785 and 1320, 2420 and 20500, min. 2690 and 890).

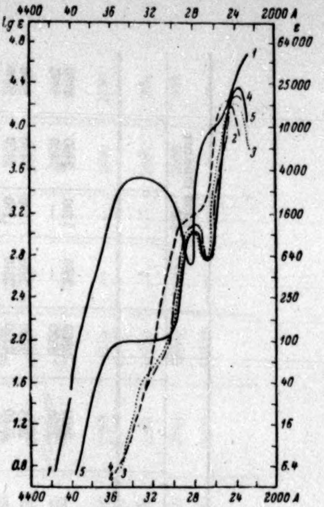

Fig. 4. m-Aminoacetophenone in different solvents. 1) In water ($2 \cdot 10^{-2}$-$2 \cdot 10^{-5}$ M) (max. 3335 and 3170, inflection 2540 and 10000, min. 2850 and 600); 2) in 38.1% hydrochloric acid; 3) in 13.6% hydrochloric acid; 4) in 0.7% hydrochloric acid ($2 \cdot 10^{-2}$-$2 \cdot 10^{-5}$ M) (inflection 3050 and 100, max. 2800 and 1260, 2385 and 20500, min. 2670 and 590); 5) in 0.07% hydrochloric acid ($2 \cdot 10^{-2}$-$2 \cdot 10^{-5}$ M) (inflection 3300 and 100, max. 2800 and 1050, 2325 and 20500, min. 2685 and 590).

in concentrated H_2SO_4 are given in Reference [10]. Both m- and p-aminoacetophenones give weak long wavebands at $\lambda = 3930$ A (ϵ 60) and 3945 A (ϵ 10), corresponding to the series of bands of unsubstituted acetophenone in concentrated H_2SO_4 [11].

A different behavior is shown in dilute sulfuric acid (17.6%). In this case, as in aqueous HCl, all the isomers behave similarly; their curves are considerably displaced towards shorter wavelength, and nearly coincide with each other and with that for unsubstituted acetophenone in water (Figure 9). For all the isomers, further dilution of the sulfuric acid to a concentration of 0.2% causes the same effect as the dilution of hydrochloric acid to 0.7%, namely a shift of the maxima and limits of the long wavebands to shorter wavebands. This effect is again least pronounced with the meta isomer, a fact which is obviously connected with the great stability of the salt of the latter.

The N-acetylaminoacetophenones in 99.8% H_2SO_4 (Figure 10) show some special features not found with the aminoacetophenones. The absorption curves of the meta and para isomers are different. The spectrum of m-N-acetylaminoacetophenone is similar as regards number and position of bands to that of acetophenone in concentrated H_2SO_4, but the spectrum of p-N-acetylaminoacetophenone resembles that of acetophenone in water. The absorption curve of the ortho isomer is similar to that of unsubstituted acetophenone in water, with the difference that the intensities of all three bands are 5 to 10 times greater.

TABLE 1

N-Acetylaminoacetophenones in Aqueous HCl

$CH_3CONHC_6H_4COCH_3$	Solvent	Band maxima						Band minima			
		λ	ε	λ	ε	λ	ε	λ	ε	λ	ε
Ortho-	H_2O	3230	4270	—	—	2600	12900	2805	1780	2460	8920
	38.1% HCl	3100 (Inflection)	1080	—	—	2560	8520	—	—	2450	5890
	13.6% HCl	3225	3390	—	—	2615	9030	2835	1180	2480	5890
	0.7% HCl	3230	3170	—	—	2580	6310	2840	1150	2450	5000
Meta-	H_2O	3015	1870	—	—	2580 (Inflection)	18600	2770	760	—	—
	38.1% HCl	2890 (Inflection)	1740	—	—	2440	31000	—	—	—	—
	13.6% HCl	2980	1590	—	—	2450	20500	2810	760	—	—
	0.7% HCl	3000	1910			2425 (Inflection)	42700	2775	890	—	—
Para-	H_2O	—	—	2815	63100	—	—	—	—	—	—
	38.1% HCl	—	—	2765	15900	—	—	—	—	—	—
	13.6% HCl	—	—	2805	31700	2600 (Inflection)	6770	—	—	2390	2960
	0.7% HCl	—	—	2820	25200	—	—	—	—	—	—
$C_6H_5COCH_3$	H_2O	3325	50	2800 (Inflection)	1150	2495	11000	—	—	—	—

TABLE 2

N, N-Dimethylaminoacetophenones in Aqueous HCl

$(CH_3)_2NC_6H_4COCH_3$	Solvent	Band Maxima						Band Minima			
		λ	ε	λ	ε	λ	ε	λ	ε	λ	ε
Ortho -	H_2O	3750	3990	—	—	2660	5000	3010	775	2595	4370
	38.1% HCl	—	—	2830 (inflection)	1780	2440	20900	—	—	—	—
	13.6% HCl	3160 (inflection)	60	2840	2050	2440	10500	—	—	2695	1150
	0.7% HCl	3150 (inflection)	75	2825	1630	2450	21400	—	—	2710	1150
	0.07% HCl	3790	110	2815	2090	2415	17000	3005	750	2660	1200
Meta -	H_2O	3550	2140	—	—	2420	39900	2955	760	—	—
	38.1% HCl	—	—	2800 (inflection)	1130	2420	18700	—	—	—	—
	13.6% HCl	3190 (inflection)	55	2805	1050	2410 (inflection)	20000	—	—	2660	760
	0.7% HCl	3135 (inflection)	65	2780	1080	2375	61300	—	—	2635	775
Para -	H_2O	—	—	3435	39900	2380	6310	—	—	2680	1180
	38.1% HCl	—	—	2770 (inflection)	1910	2440	21400	—	—	—	—
	13.6% HCl	3165 (inflection)	70	2795	1660	2395	39900	—	—	2665	890
	0.7% HCl	3415	660	2790	1555	2385	45800	3065	290	2660	955
Acetophenone	H_2O	3225	50	2800 (inflection)	1150	2495	11000	—	—	—	—

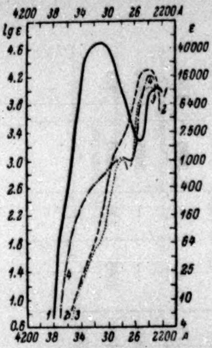

Fig. 5. p-Aminoacetophenone in different solvents. 1) In water ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M) (max. 3115 and 56300, 2325 and 10800, min. 2525 and 1910); 2) in 38.1% hydrochloric acid; 3) in 13.6% hydrochloric acid; 4) in 0.7% hydrochloric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M) (inflection 3250 and 445, max. 2760 and 1260, 2355 and 20000, min. 2660 and 1080).

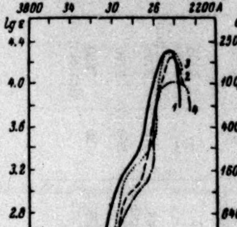

Fig. 7. N,N-Dimethylaminoacetophenones in 38.1% hydrochloric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) o-Dimethylaminoacetophenone; 2) m-dimethylaminoacetophenone; 3) p-dimethylaminoacetophenone; 4) acetophenone in water [8] (for data on max. and min. see Table 2).

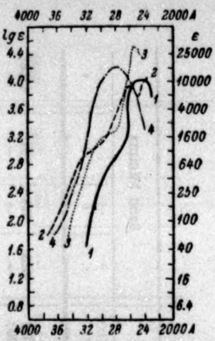

Fig. 6. N-Acetylaminoacetophenone in 38.1% hydrochloric acid ($2\cdot10^{-3}$-$2\cdot10^{-5}$ M). 1) Acetophenone in water [8]; 2) o-N-acetylaminoacetophenone; 3) m-N-acetylaminoacetophenone; 4) p-N-acetylaminoacetophenone (see Table 1 for data on max. and min.).

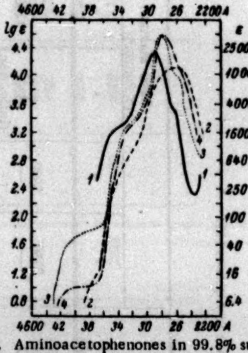

Fig. 8. Aminoacetophenones in 99.8% sulfuric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) Acetophenone in 95.99% sulfuric acid [10] (10^{-3}-10^{-5} M) (inflection 3300 and 2400, max. 2950 and 20500); 2) o-aminoacetophenone (inflection 3260 and 780, max. 2645 and 12900); 3) m-aminoacetophenone (inflection 3930 and 60, 3250 and 2400, max. 2810 and 4000); 4) p-aminoacetophenone (inflections 3945 and 10, 3220 and 2400, max. 2790 and 38900).

The absorption curves of the N,N-dimethylaminoacetophenones in 99.8% H_2SO_4 are considerably displaced towards shorter wavelength compared

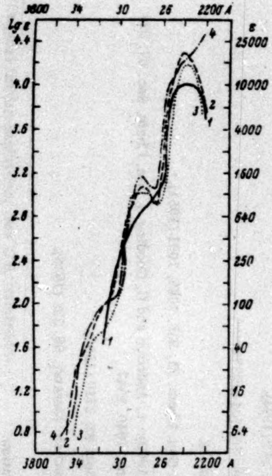

Fig. 9. Aminoacetophenones in aqueous sulfuric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) Acetophenone in water [8]; 2) o-aminoacetophenone in 17.5% sulfuric acid (inflection 3150 and 100, max. 2795 and 1205, 2415 and 18060, min. 2700 and 905); 3) m-aminoacetophenone in 17.5% sulfuric acid (inflection 3120 and 65, max. 2805 and 1080, 2390 and 15900, min. 2660 and 900); 4) p-aminoacetophenone in 17.5% sulfuric acid (inflection 3110 and 110, max. 2805 and 1555, inflection 2375 and 19500, min. 2695 and 1130).

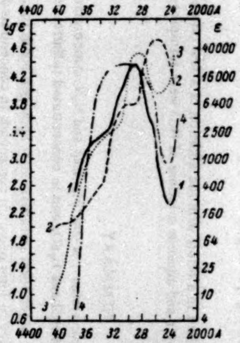

Fig. 10. N-Acetylaminoacetophenones in 99.8% sulfuric acid. 1) Acetophenone in 95.99% sulfuric acid [10]; 2) ortho- ($2\cdot10^{-3}$-$2\cdot10^{-5}$ M) (inflections 3340 and 500, 2950 and 6020, max. 2575 and 52500); 3) meta- ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M) (inflection 3285 and 2240, max. 2845 and 33200); 4) para- ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M) (max. 3045 and 23000).

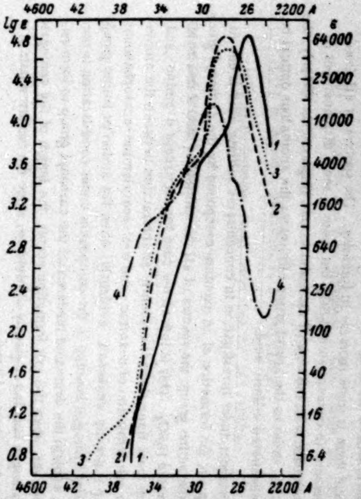

Fig. 11. N,N-Dimethylaminoacetophenones in 99.8% sulfuric acid ($2\cdot10^{-2}$-$2\cdot10^{-5}$ M). 1) Ortho- (inflection 3040 and 3890, max. 2580 and 63200); 2) meta- (inflection 3150 and 3550, max. 2780 and 63100); 3) para- (inflections 3850 and 10, 3145 and 3720, max. 2770 and 45800); 4) acetophenone in 95.99% sulfuric acid [10].

with those of the aqueous solutions. The displacement of the long-wave maximum is 710 A for the ortho, 400 A for the meta, and 665 A for the para isomer, and there is some increase in intensity. The spectra of all three isomers resemble that of unsubstituted acetophenone in concentrated H_2SO_4, but there is some displacement of all three curves towards shorter wavelength, particularly in the case of the ortho isomer (Figure 11). Clearly, the presence of $N(CH_3)_2$, instead of NH_2 or $NHCOCH_3$, ortho to the acetyl group eliminates the anomalous optical behavior of the ortho isomers with respect to concentrated sulfuric acid.

As stated above, the behavior of the substances under investigation in concentrated sulfuric acid is due to two effects: salt formation by the amino group and the formation of an oxonium compound by the carbonyl group. Because salt formation removes the effect of the amino group, the spectra of all the substances should resemble that of unsubstituted acetophenone in concentrated H_2SO_4. This is indeed the case for all except o-amino- and o- and p-N-acetylamino-acetophenones. With these three there is evidently an interaction between the amino and carbonyl group. When there is noticeable salt formation of o-amino- and o-N-acetylamino-acetophenones the interaction of acid with the carbonyl group is greatly weakened. Evidently, when the amino or imino groups form salts in concentrated H_2SO_4, intramolecular hydrogen bonding in the compounds under consideration is not completely prevented, and this may, perhaps, explain the decreased tendency of the carbonyl group to form oxonium compounds in concentrated H_2SO_4. However, when this salt formation occurs, the length of the conjugate system is reduced, and the optical effect of hydrogen bonding is greatly diminished, since the unshared pair of electrons on the nitrogen atom becomes involved in chemical bonds.

EXPERIMENTAL

The method of measuring the spectra and the synthesis and purification of the substances investigated have been described previously [9].

Hydrochloric acid was prepared by saturating spectrographically pure water with hydrogen chloride, obtained from NaCl and H_2SO_4.

Chemically pure sulfuric acid was distilled in a retort with the addition of a few crystals of sodium nitrate. Concentrated sulfuric acid, its solutions in water and aqueous solutions of HCl were transparent down to 2100 A, in a cell 5 cm thick exposed for 10 seconds.

SUMMARY

1. The ultraviolet spectra of the isomeric amino-, N-acetylamino and N,N-dimethylamino-acetophenones have been investigated in aqueous solutions of HCl and H_2SO_4 and in concentrated sulfuric acid.

2. It has been found that the substances which form intramolecular hydrogen bonds (o-amino- and o-N-acetylamino-acetophenones) show less tendency to form oxonium compounds in concentrated sulfuric acid.

3. It is suggested that salt formation by the amino or imino groups greatly diminishes the optical effect of intramolecular hydrogen bonding, but does not necessarily eliminate it.

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DIHYDROSARCOMYCIN AND RELATED COMPOUNDS. I.

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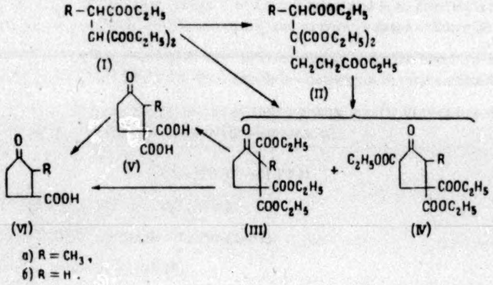
Very recently reports have appeared in the literature on the isolation of a new antibiotic, sarcomycin, which retards the development of some types of malignant tumors [1]. The antibiotic was not isolated in a separate state; however, on the basis of some of its reactions, it was given the structure of 2-methylenecyclopentanone-3-carboxylic acid. It was noted that the corresponding dihydro derivative – 2-methylcyclopentanone-3-carboxylic acid – also possessed anti-tumor activity. In connection with this, it seemed worthwhile to develop a convenient method for synthesizing this dihydro derivative and its lower homolog – cyclopentanone-3-carboxylic acid – and also to elucidate certain stereochemical questions on the first of these compounds. The present report is devoted to the solution of these problems.

Several different syntheses of 2-methylcyclopentanone-3-carboxylic acid are described in the literature [2-4]; however, all of them have many stages and they suffer from a series of preparative difficulties, in particular, certain stages of the process require a great deal of time.

The method we used was found to be more convenient (see note at end of article); it can be expressed by the following scheme:



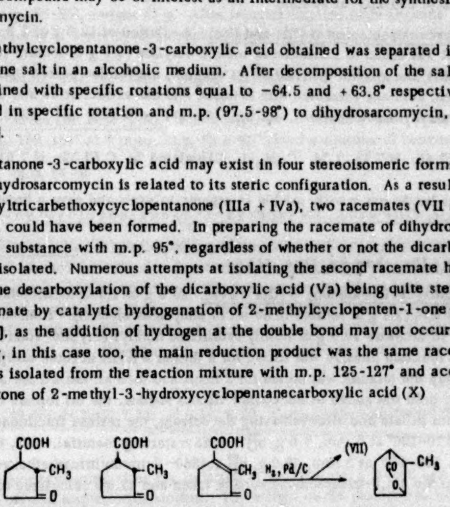
Condensation of 1,1,2-tricarbethoxypropane (Ia) with methyl acrylate gave 1,3,3,4-tetracarbethoxypentane (IIa), which had been prepared previously by another method [5]. Cyclization of (IIa) by heating it with sodium alcoholate resulted in tricarbethoxymethylcyclopentanone, which is, apparently, a mixture of both possible forms (IIIa and IVa), which on subsequent treatment form the same reaction product. We found the conditions under which the stages of the Michaelis condensation and cyclization could be combined successfully. In this case, the mixture of isomeric 2-methyltricarbethoxycyclopentanones (IIIa and IVa) was obtained directly from tricarbethoxypropane (Ia) in a yield higher than 80%, calculated on the amount of (Ia) reacting. An essential condition for the successful use of this method is strict adherence to the temperature schedule of the reaction – the first period at room temperature is necessary for completion of the Michaelis condensation and the subsequent heating produces cyclization.

On heating the mixture of (IIIa) and (IVa) with dilute hydrochloric acid solution, ketonic cleavage of the β-keto ester grouping occurs simultaneously with hydrolysis of the gem-carbethoxy groups and, as a result, the same 2-methylcyclopentanone-3-dicarboxylic acid (Va) is formed from both of the isomers (IIIa) and (IVa). When heated to 160-170°, this product readily loses one carboxyl group and is converted into the racemate of dihydrosarcomycine (VIa) with m.p. 95°. This substance may be prepared without isolating the dicarboxylic acid (Va), by heating a mixture of isomers (IIIa) and (IVa) with a mixture of concentrated hydrochloric acid and acetic acids and subsequently distilling the reaction product. Thus, racemic dihydrosarcomycin may be prepared from the tricarbethoxy derivative (Ia) by a two-stage synthesis.

We also used the method of synthesis developed for preparing the lower analog of dihydrosarcomysin-cyclopentanone-3-carboxylic acid (VIb, R = H), which had been prepared previously by Perkin, using a more complicated method [6]. This compound may be of interest as an intermediate for the synthesis of a series of derivatives or analogs of sarcomycin.

The racemic 2-methylcyclopentanone-3-carboxylic acid obtained was separated into optical antipodes by conversion into the quinine salt in an alcoholic medium. After decomposition of the salts with aqueous ammonia, two acids were obtained with specific rotations equal to −64.5 and +63.8° respectively (c 2.5 in water); the second acid corresponded in specific rotation and m.p. (97.5-98°) to dihydrosarcomycin, obtained by reduction of the natural antibiotic [1].

2-Methylcyclopentanone-3-carboxylic acid may exist in four stereoisomeric forms; it is possible that the biological activity of dihydrosarcomycin is related to its steric configuration. As a result of hydrolysis and decarboxylation of 2-methyltricarbethoxycyclopentanone (IIIa + IVa), two racemates (VII and VIII), belonging to the cis- and trans-series, could have been formed. In preparing the racemate of dihydrosarcomycin (VIa), we always isolated the same substance with m.p. 95°, regardless of whether or not the dicarboxylic acid (Va) formed as an intermediate, was isolated. Numerous attempts at isolating the second racemate have so far been unsuccessful, apparently, due to the decarboxylation of the dicarboxylic acid (Va) being quite stereospecific. We tried to prepare the second racemate by catalytic hydrogenation of 2-methylcyclopenten-1-one-3-carboxylic acid (IX), described by Newman [4], as the addition of hydrogen at the double bond may not occur stereochemically symmetrically [7]. However, in this case too, the main reduction product was the same racemate with m.p. 95°; in addition, a substance was isolated from the reaction mixture with m.p. 125-127° and according to analysis and properties it was the lactone of 2-methyl-3-hydroxycyclopentanecarboxylic acid (X)



(VII) (VIII) (IX) (X)

In order to establish which of the steric configurations (VII) or (VIII), is that of 2-methylcyclopentanone-3-carboxylic acid (dihydrosarcomycin, VI), we reduced the carbonyl group in it by Kischner's method, and converted the 2-methylcyclopentanecarboxylic acid obtained into the amide. This amide did not depress the melting point of the amide of trans-2-methylcyclopentanecarboxylic acid [8, 9]. From this one can conclude that 2-methylcyclopentanone-3-carboxylic acid with m.p. 95° and dihydrosarcomycin, obtained by hydrogenation of the natural antibiotic sarcomycin, are of the trans-series.

EXPERIMENTAL

1,3,3,4-Tetracarbethoxypentane (IIa). 29.0 g of 1,1,2-tricarbethoxypropane (prepared according to [10], yield 90%, b.p. 108-111° at 4 mm, n_D^{20} 1.4295) was added to a solution of sodium ethylate (0.5 g of sodium in 50 ml of anhydrous alcohol), the mixture was cooled to 5-10° and 10.0 g of freshly distilled methyl acrylate was added dropwise over a period of 5-10 minutes with vigorous stirring. The mixture was stirred at 5-10° for 30 minutes; it was left at room temperature for 24 hours, after which 150 ml of water was added followed by 2 N sulfuric acid until it was acid to congo. The oil formed was separated, the aqueous layer extracted twice with ether and the extracts combined with the main portion of the substance and dried over sodium sulfate. After distilling off the solvent, the residue was fractionated in vacuum. We obtained fractions: 1st, b.p. 110-120° at 4 mm, 4.0 g, n_D^{20} 1.4320 – starting material; 2nd b.p. 165-168° at 3 mm, 24.0 g, n_D^{20} 1.4480 – a colorless, viscous liquid, which was insoluble in water and did not give a color with ferric chloride in methanol solution – 1,3,3,4-tetracarbethoxypentane. The yield was 66.7%, calculated on the 1,1,2-tricarbethoxypropane taken.

Found %: C 56.37; H 8.02. $C_{17}H_{28}O_8$. Calculated %: C 56.65; H 7.77.

Literature data [5]: b.p. 222° at 12 mm.

1,2,2,4-Tetracarbethoxybutane (IIb). This was prepared similarly from 15.2 g of 1,1,2-tricarbethoxyethane [11] and 6.0 g of methyl acrylate in 25 ml of anhydrous alcohol in the presence of sodium ethylate (0.1 g of sodium). The yield was 15 g (71.4%); the b.p. was 158-160° at 1 mm; n_D^{20} 1.4438.

Literature data [6]: b.p. 200-203° at 12 mm.

2-Methyltricarbethoxycyclopentanone-3 (IIIa and IVa). A solution of 12.0 g of 1,3,3,4-tetracarbethoxypentane in 15 ml of alcohol was added to a solution of sodium ethylate (0.9 g of sodium in 35 ml of alcohol), the mixture boiled for 4 hours, the alcohol distilled off in vacuum, the residue poured into water, the solution neutralized with hydrochloric acid and extracted with benzene and the extract dried and distilled; we obtained 3.3 g of 2-methyltricarbethoxycyclopentanone-3 with b.p. 172-174° at 5 mm; n_D^{20} 1.4540.

Found %: C 57.58, 57.43; H 7.13, 7.14. $C_{15}H_{22}O_7$. Calculated %: C 57.32; H 7.01.

The colorless, viscous liquid was readily soluble in organic solvents and gave a brown color with a solution of ferric chloride in methanol.

Condensation and Cyclization in One Stage

A. 2-Methyltricarbethoxycyclopentanone-3 (IIIa + IVa). 29.0 g of 1,1,2-tricarbethoxypropane was added to a solution of sodium ethylate (2.3 g of sodium in 50 ml of anhydrous alcohol). Then the mixture was cooled to 10-15° and to it was added dropwise 10.0 g of freshly redistilled methyl acrylate, stabilized with hydroquinone, with vigorous stirring. The reaction mixture was stirred for a further 2 hours at room temperature and then left overnight. The following day the mixture was boiled for 3 hours and then almost all the alcohol distilled off (45 ml). 100 ml of 2 N sulfuric acid was added to the cooled viscous residue, the oil formed extracted with ether, the extract dried with sodium sulfate and after removing the solvent, the residue fractionated in vacuum. We obtained fractions: 1st, b.p. 110-120° at 4 mm, 7.0 g, n_D^{20} 1.4325 – starting material; 2nd, b.p. 120-158° at 3 mm, 3.0 g, n_D^{20} 1.4419; 3rd, b.p. 158-160° at 3 mm, 19.0 g, n_D^{20} 1.4560– 2-methyltricarbethoxycyclopentanone-3. The yield was 61% calculated on the 1,1,2-tricarbethoxypropane taken and 81.5% calculated on that which reacted.

Found %: C 57.30, 57.25; H 7.12, 7.33. $C_{15}H_{22}O_7$. Calculated %: C 57.31; H 7.07.

B. Tricarbethoxycyclopentanone (IIIb + IVb). As described above, from 30.0 g of 1,1,2-tricarbethoxyethane and 12.5 g of methyl acrylate in 50 ml of alcohol in the presence of sodium ethylate (from 3.0 g), after fractionation we obtained 25.8 g (67%) of tricarbethoxycyclopentanone with b.p. 180-185° at 5 mm, n_D^{20} 1.4558. The colorless, viscous liquid gave a brown color with ferric chloride in methanol solution; it was hydrolyzed and decarboxylated without additional purification.

2-Methylcyclopentanone-3-dicarboxylic-1,1-acid (Va). A mixture of 5% hydrochloric acid solution and the isomeric 2-methyltricarbethoxycyclopentanones-3 (IIIa and IVa) was boiled for 6 hours. The crystals, which separated on cooling, were filtered off and dried in vacuum over phosphorus pentoxide. The yield was 13.1 g (44.2%); the m.p. 158° (with decomposition).*

Found %: C 51.53, 51.65; H 5.65, 5.72. $C_8H_{10}O_5$. Calculated %: C 51.61; H 5.38.

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*Here and later on uncorrected melting points are reported.

2-Methylcyclopentanone-3-carboxylic Acid (the racemate of dihydrosarcomycin) (VIa).

a) Decarboxylation of 2-methylcyclopentanone-3-dicarboxylic acid. 10 g of the dicarboxylic acid was slowly heated to 160°; after the evolution of the bulk of the carbon dioxide, the mixture was heated quickly to 250°. We obtained 7.5 g of an impure acid, which had m.p. 89° after pressing on porous plate and melted at 93-94° after recrystallization from benzene. Literature data [2]: m.p. 95°.

b) Hydrolysis and decarboxylation of the mixture of isomeric 2-methyltricarbethoxycyclopentanones-3 (IIIa + IVa). A mixture of 165 g of 2-methyltricarbethoxycyclopentanone, 510 ml of concentrated hydrochloric acid and 170 ml of acetic acid was boiled under reflux for 1 hour, after which a mixture of ethyl acetate and acetic acid was distilled off up to a temperature of 107-110° (in steam). 100 ml of hydrochloric acid and 100 ml of acetic acid were added and the treatment described above repeated with the difference that the distillation was continued until the residue had a sirupy consistency and crystallized completely on cooling. The residue was heated at 160-200° under 10-15 mm pressure until it no longer frothed and was distilled in vacuum; b.p. 141-142° at 3 mm, m.p. 80-85°, weight 51 g. After recrystallization from benzene and washing with cold ether, we obtained 38 g (51.5%) of 2-methylcyclopentanone-3-carboxylic acid, m.p. 94.5-95°.

Found %: C 59.25, 59.28; H 7.12, 7.01. $C_7H_{10}O_3$. Calculated %: C 59.15; H 7.09.

Cyclopentanone-3-carboxylic acid (VIb). This was prepared similarly from tricarbethoxycyclopentanone. The yield was 76.8%; b.p. 152-154° at 4 mm; m.p. 63.5-65° (from a mixture of benzene and petroleum ether).

Literature data [6]: m.p. 64-65°.

Resolution of 2-Methylcyclopentanone-3-carboxylic Acid into Optical Antipodes

a) Preparation of quinine salts. A solution of 5 g of the racemic 2-methylcyclopentanone-3-carboxylic acid in 15 ml of anhydrous alcohol was mixed with a hot solution of 12.15 g of quinine. The mixture was heated to boiling and left for 2 hours at room temperature. The precipitate was filtered off and washed with cold alcohol (5 ml). The weight of the residue was 9.2 g, m.p. 162-163°, $[\alpha]_D^{20}$ $-127.4°$ (c 2, in water). The salt obtained (9.2 g) was recrystallized from 30 ml of anhydrous alcohol; we obtained 5.85 g of a salt, m.p. 169-170° $[\alpha]_D^{20}$ $-153.2°$ (c 2, in water). Repeated crystallization did not change the melting point or the specific rotation of the salt.

Found %: C 69.63, 69.66; H 7.47, 7.51; N 6.10, 6.29. $C_{27}H_{34}O_5N_2$. Calculated %: C 69.52; H 7.29; N 6.01.

From the mother liquor remaining after the isolation of the first salt a second salt precipitated after 24 hours, which was filtered off and washed with alcohol. The weight of the precipitate was 3.8 g, m.p. 167-168°, $[\alpha]_D^{20}$ $-93.8°$ (c 3, in water). After recrystallization from 8 ml of anhydrous alcohol, we obtained 3.3 g of a salt, m.p. 168-169°, $[\alpha]_D^{20}$ $-93.5°$ (c 3, in water).

Found %: C 69.65, 69.58; H 7.50, 7.45; N 5.94, 5.87. $C_{27}H_{34}O_5N_2$. Calculated %: C 69.52; H 7.29; N 6.01.

b) Isolation of the optically active acids. A 10% ammonia solution was added to a solution of 5.3 g of the first salt ($[\alpha]_D^{20}$ $-153.2°$) in 235 ml of water until the quinine was completely precipitated. The precipitated quinine was filtered off, weight 3.4 g (calculated 3.56 g) and the aqueous solution twice extracted with ether, concentrated in vacuum, acidified with sulfuric acid solution and saturated with magnesium sulfate. The acid separated as an oil, which quickly crystallized. The acid was extracted with ether, the ether solution dried with magnesium sulfate and the ether evaporated off. The residue (1.4 g) was recrystallized from 4 ml of benzene; we obtained 0.85 g of the (−)-acid, m.p. 98-98.5°, $[\alpha]_D^{20}$ $-64.5°$ (c 2.5, in water).

Found %: C 59.40, 59.21; H 7.05, 7.18. $C_7H_{10}O_3$. Calculated %: C 59.15; H 7.09.

Similarly, from 3 g of the second salt ($[\alpha]_D^{20}$ $-93.5°$) we isolated 1 g of an acid, which was recrystallized from benzene and washed with petroleum ether (b.p. 30-60°); we obtained 0.55 g of the (+)-acid, m.p. 97.5-98.0°, $[\alpha]_D^{20}$ +63.8° (c 2.5, in water).

Found %: C 59.30, 59.40; H 7.20, 7.21. $C_7H_{10}O_3$. Calculated %: C 59.15; H 7.09.

Literature data [1] for dihydrosarcomycin, prepared by reduction of the natural antibiotic: m.p. 99-99.5°, $[\alpha]_D^{20}$ +66.7° (c 1, in water).

50 mg of the (−)-acid (m.p. 98.0-98.5°) was mixed with 50 mg of the (+)-acid (m.p. 97.5-98.0°) and the mixture recrystallized from benzene. The acid obtained was optically inactive and had m.p. 94-95°.

Catalytic reduction of 2-methylcyclopenten-1-one-3-carboxylic acid. A solution of 1 g of 2-methylcyclopenten-1-one-3-carboxylic acid [4] in 50 ml of anhydrous alcohol was hydrogenated over palladium on charcoal (0.25 g, 20% Pd) at room temperature with a slight excess pressure of hydrogen. After the absorption of 1 mole of hydrogen (170 ml) the reduction was stopped, the catalyst filtered off and the alcohol solution evaporated to dryness in vacuum. We obtained 0.9 g of a thick, viscous oil, which partially crystallized on standing. 3 ml of water was added and the crystals (well-formed rhombs) were filtered off, washed with water and dried. We obtained 20 mg of a substance with m.p. 125-127° with the properties of a lactone. It was readily soluble in organic solvents, difficultly in water, insoluble in sodium bicarbonate solutions and soluble in caustic alkalis.

Found %: C 66.76, 66.79; H 7.94, 7.91. $C_7H_{10}O_2$. Calculated %: C 66.66; H 8.00.

After the separation of the lactone, the mother liquor was saturated with ammonium sulfate and extracted several times with ether. The ether solution was dried over magnesium sulfate and evaporated down. We obtained 0.6 g of an acid with m.p. 88-90°. After recrystallization from petroleum ether we obtained 0.3 g of an acid with m.p. 91-92.5°. A mixture with 2-methylcyclopentanone-3-carboxylic acid melted at 92.5-93°.

Reduction of 2-methylcyclopentanone-3-carboxylic acid by Kischner's method. A mixture of 1 g of 2-methylcyclopentanone-3-carboxylic acid, 2 g of sodium hydroxide, 2 ml of hydrazine hydrate and 75 ml of diethylene glycol was heated under reflux for 6 hours at 220-230°; on cooling, 150 ml of water was added, the aqueous layer twice extracted with ether and acidified with hydrochloric acid and after this the 2-methylcyclopentanecarboxylic acid was extracted several times with ether. After removing the solvent, we obtained 0.7 g of a liquid acid, which was heated with 3 ml of thionyl chloride for 4 hours at 40°. After removing the thionyl chloride, the acid chloride obtained was dissolved in benzene, saturated with dry ammonia, the ammonium chloride precipitate filtered off and the filtrate evaporated to dryness and extracted with ether. After evaporating off the ether, the residue was sublimed. The amide obtained had m.p. 149-150° and did not depress the melting point of the amide of trans-2-methylcyclopentanecarboxylic acid [8, 9].*

SUMMARY

1. A convenient method has been developed for the synthesis of cyclopentanone-3-carboxylic acids, by condensation of methyl acrylate with appropriate 1,1,2-tricarbethoxyalkanes, with simultaneous cyclization into cyclopentanone derivatives and subsequent hydrolysis and decarboxylation.

2. The 2-methylcyclopentanone-3-carboxylic acid obtained was separated into optical antipodes, of which the (+)-isomer corresponded in its properties to dihydrosarcomycin obtained by reduction of natural sarcomycin.

3. It was shown that dihydrosarcomycin has a trans configuration.

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*The method described here is the content of the invention, described in Author's Certificate No. 19/2478 (USSR Ministry of Health) with priority from February 3rd, 1956.

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*Russian translation.

HALOGENATION OF AROMATIC SILANES

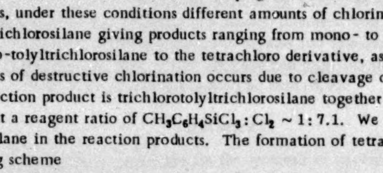
IV. PREPARATION AND PROPERTIES OF CHLORO AND BROMO DERIVATIVES OF p-TOLYLTRICHLOROSILANE

G.V. Motsarev and A.Ya. Yakubovich

We showed previously [1] that in the halogenation of phenyltrichlorosilane in the presence of catalysts, the $SiCl_3$ group, which by nature is meta directing, directed the halogen atoms entering the nucleus into the para- and ortho-positions. It seemed interesting to determine the directing effect of the $SiCl_3$ group when there were present in the aromatic nucleus of the silane other substituents – directors of the first or second type. For this purpose we investigated the halogenation of p-tolyltrichlorosilane, which has in the para-position in the nucleus a methyl group, that is a director of the first type. We were unable to find any information in the literature on the halogenation of this silane and therefore the reaction was fully investigated.

The chlorination and bromination of p-tolyltrichlorosilane was investigated under various temperature conditions (20-100°), at various molar ratios of silane to halogen, with and without catalysts (metallic iron, antimony trichloride).

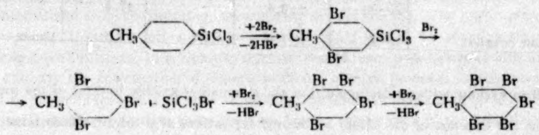
It was established that an energetic exothermic reaction occurs which proceeds vigorously even at 20-25°, when p-tolyltrichlorosilane is treated with chlorine in the presence of metallic iron or $SbCl_3$. Depending on the molar ratio of the reagents, under these conditions different amounts of chlorine could be substituted in the aromatic nucleus of p-tolyltrichlorosilane giving products ranging from mono- to trichloro derivatives in yields of 82-89%. In chlorinating p-tolyltrichlorosilane to the tetrachloro derivative, as in the halogenation of phenylchlorosilanes [2], a process of destructive chlorination occurs due to cleavage of the silane molecule at the C–Si bond. Thus, the main reaction product is trichlorotolyltrichlorosilane together with $SiCl_4$ and a mixture of tetra- and pentachlorotoluenes at a reagent ratio of $CH_3C_6H_4SiCl_3 : Cl_2 \sim 1 : 7.1$. We were completely unable to detect tetrachlorotolyltrichlorosilane in the reaction products. The formation of tetra- and pentachlorotoluenes could be expressed by the following scheme



This scheme was confirmed by experiments on the chlorination of trichlorotolyltrichlorosilane. Its chlorination (at a reagent ratio $CH_3C_6HCl_3SiCl_3 : Cl_2 \sim 1 : 2$) in the presence of metallic iron at 90-95° gave a mixture of tetra- and pentachlorotoluenes.

The C–Si bond is cleaved more readily by chlorine in p-tolyltrichlorosilane than in the chlorination of phenyltrichlorosilane. Thus, in the chlorination of phenyltrichlorosilane in the presence of $FeCl_3$, this reaction can hardly be observed even at a temperature of 140-150° while in the presence of $SbCl_3$ it does not occur at all, whereas in the case of p-tolyltrichlorosilane the process of destructive chlorination proceeds both in the presence of $FeCl_3$ and $SbCl_3$ and at lower temperatures (90-100°). The higher sensitivity of the C–Si bond in p-tolyltrichlorosilane to cleavage as compared with that in phenyltrichlorosilane is similar to the known cases of cleaving the C–Si bond in aromatic silanes [p-$CH_3OC_6H_4Si(CH_3)_3$] in an aqueous methanol solution of hydrochloric acid [3]. The cleavage is facilitated by the presence of substituents of the first type in the position para to the C–Si bond.

The bromination of p-tolyltrichlorosilane was carried out under the same conditions as the chlorination. It was established that bromination proceeded quite vigorously at 20-25° and under these conditions, depending on the molar ratio of reagents, products of mono- and dibromo substitution in the aromatic nucleus of p-tolyltrichlorosilane may be obtained in an 80-90% yield. Increasing the bromination temperature to 70-80° (molar ratio of reagents 1:2.2) resulted in a decreased yield of dibromotolyltrichlorosilane (from 84-91 to 81-82%) due to the appearance of a side process – cleavage of the reaction products formed. This tendency in the reaction was found to dominate in attempts to prepare tribromotolyltrichlorosilane. In this case (molar ratio of $CH_3C_6H_4SiCl_3 : Br_2 \sim 1:3.4$) the main reaction products were $SiCl_3Br$ and a mixture of tri-, tetra- and pentabromotoluenes, besides dibromotolyltrichlorosilane, which was obtained in 47.4% yield. This bromination of p-tolyltrichlorosilane proceeds by the scheme



The effects of catalysts, reagent ratios and temperature on the results of the chlorination and bromination of p-tolyltrichlorosilane are illustrated by the data given in Tables 1 and 2.

It was found that in the chlorination and bromination of p-tolyltrichlorosilane in the presence of catalysts, discrete compounds, namely 3-chloro(bromo)-4-methylphenyltrichlorosilanes, were formed only in the case of monochloro- and monobromo derivatives. Mixtures of isomers of di- and trihalo derivatives are formed by more drastic halogenation.

TABLE 1

The Effect of Catalysts,* Reagent Ratio and Temperature on the Chlorination of p-Tolyltrichlorosilane

Expt. No.	Conditions of p-tolyltrichlorosilane chlorination			Composition of reaction products			Percent of silane cleaved
	catalyst	temperature	molar ratio $C_7H_7SiCl_3 : Cl_2$	unchanged silane (in %)	chlorination products		
					total yield (in %)	main reaction product	
1	SbCl₃	22-50°	1:1.0	7.0	84.7	Mono-	–
2		50-70	1:1.9	–	82.8	Di-	–
3		50-80	1:3.0	–	89.0	Tri-	–
4		70-100	1:7.1	–	70.7	Tri-	15.7
5	Fe metal	20-25	1:1.8	–	83.7	Mono-, di-	–
6		20-25	1:3.4	–	82.6	Tri-	–
7		70-85	1:2.6	–	85.7	Di-	–
8		20-90	1:6.8	–	73.0	Tri-	6.6
9	Without catalyst	20-25	1:9.1	97.2	–	–	–
10		95-100	1:8.0	27.5	51.0	Mono-	–

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*In all the experiments, the amount of catalyst was 0.5% (of the weight of silane taken).

The mono- and dichloro derivatives of p-tolyltrichlorosilane are colorless mobile oily liquids; the monobromo derivative is a liquid which slowly crystallizes on standing (plates); the trichloro and dibromo derivatives are white crystalline materials (needles). All the chloro- and bromotolyltrichlorosilanes have a sharp smell,

TABLE 2

Effect of Catalysts, Reagent Ratio and Temperature on the Bromination of p-Tolyltrichlorosilane

Expt. No.	Conditions of p-tolyltrichlorosilane bromination			Composition of reaction products			Percent of silane cleaved
	catalyst	temperature	molar ratio $C_7H_7SiCl_3 : Cl_2$	unchanged silane (in %)	bromination products		
					total yield (in %)	main reaction product	
1	Fe metal	25-32°	1:1.1	4.5	80.2	Mono-	–
2		15-20	1:1.1	4.7	83.2	"	–
3		25-40	1:2.2	–	91.4	Di-	–
4		20-25	1:2.1	–	84.6	"	–
5		40-70	1:2.1	–	82.4	"	7.1
6		70-80	1:2.2	–	81.7	"	8.0
7		25-90	1:3.4	–	47.4	"	45.2
8	Without catalyst	90-95	1:1.0	30.0	52.0	Mono-	–

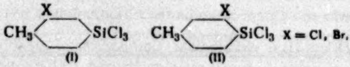
fume in air, distill in vacuum without decomposition and are readily soluble in most of the usual organic solvents.

To determine the structure of the chloro and bromo derivatives of p-tolyltrichlorosilane, as in the case of similar derivatives of phenyltrichlorosilane, we decomposed them with bromine water, which gave the corresponding chlorobromo and bromo derivatives of toluene

$$CH_3C_6H_{4-n}X_nSiCl_3 + Br_2(H_2O) \longrightarrow CH_3C_6H_{4-n}X_nBr + SiO_2 + HCl + HBr,$$

where X = Cl, Br. n = from 0 to 4.

However, by this method it was impossible to establish directly the structure of monochloro (bromo) derivatives, prepared by chlorination (bromination) of p-tolyltrichlorosilane. Actually, when the first halogen atom enters a p-tolyltrichlorosilane molecule, isomers (I) and (II) may be formed,


X = Cl, Br.

and their decomposition with bromine water should give 2-chloro(bromo)-4-bromo- and 3-chloro(bromo)-4-bromotoluenes, respectively. However, a comparison of the constants of these halo derivatives of toluene shows that they differ little from each other. Therefore, for identification of these isomers, we decided to convert them (by oxidation) into the corresponding carboxyl derivatives, namely 2-chloro(bromo)-4-bromo- and 3-chloro(bromo)-4-bromobenzoic acids, which could be readily differentiated by melting points (the melting points of 2,4- and 3,4-dibromobenzoic acids are 172-173° and 232-233° respectively).

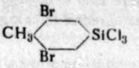
$$CH_3C_6H_{4-n}X_nBr \xrightarrow[\text{or } K_2Cr_2O_7 + H_2SO_4]{HNO_3} C_6H_{4-n}X_nBrCOOH$$

X = Cl, Br, n = from 0 to 4.

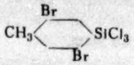
It was possible to determine the position of the halogen atoms in the aromatic nucleus of chloro- and bromotolyltrichlorosilanes and the directing effect of the substituents from the structure of these acids.

Bromine water decomposition of the monochloro- and monobromotolyltrichlorosilanes, prepared by the halogenation of p-tolyltrichlorosilane in the presence of a catalyst (iron, $SbCl_3$) gave chlorobromotoluene (in 73% yield) and dibromotoluene (76.0% yield), which when oxidized gave 2-chloro-4-bromo- and 2,4-dibromobenzoic acids (81.4 and 88.0% yields, respectively). The structure of the oxidation products isolated showed that the monochloro(bromo)-tolyltrichlorosilanes obtained were 3-chloro(bromo)-4-methylphenyltrichlorosilanes with the structure (I).

Investigation of the structures of other chloro and bromo derivatives of p-tolyltrichlorosilane showed that they were mixtures of several isomers. Thus, in decomposing dibromotolyltrichlorosilane with bromine water, the decomposition products were found to be 2,4,6- and 2,4,5-tribromotoluene with the first isomer preponderating. This showed that the dibromotolyltrichlorosilane investigated was a mixture of two isomers (III) and (IV), with a predominance of isomer (III).

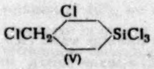


(III)



(IV)

It is known that the CH_3 group in toluene is ortho- and para-directing and activates the nucleus; the $SiCl_3$ group in phenyltrichlorosilane is meta-directing, deactivating the nucleus [4]. The introduction of a meta-directing substituent – the $SiCl_3$ group – into a toluene molecule should lead to the deactivation of the aromatic nucleus, so that p-tolyltrichlorosilane, in contrast to toluene, should react with halogens with much greater difficulty. Actually, although the chlorination of toluene without a catalyst proceeds readily even at normal temperature and results in the formation of a mixture of substitution products, containing up to four chlorine atoms in the nucleus [5], under similar conditions there is practically no chlorination of p-tolyltrichlorosilane. It can be observed only on treating p-tolyltrichlorosilane with a large excess of chlorine ($CH_3C_6H_4SiCl_3 : Cl_2 \sim 1 : 8$-9 moles) at a high temperature (95-100°), which gives a 51.0% yield of a dichloro derivative, containing 1 chlorine atom in the nucleus. Determination of its structure showed that it was 3-chloro-4-(chloromethyl)-phenyltrichlorosilane (V).

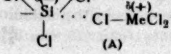


(V)

The chlorination of the methyl group of p-tolyltrichlorosilane, which takes place under the conditions indicated, may be explained by the fact that the reaction was carried out at a high temperature.

Similar results were also obtained in the bromination of p-tolyltrichlorosilane without a catalyst. In this way, the results of chlorine and bromine reactions with p-tolyltrichlorosilane without catalysts indicate that this compound behaves normally in substitution reactions in the nucleus and the halogen atom entering it is directed by both the substituents present (1-CH_3, 4-$SiCl_3$), in accordance with their nature, to position 2.

In halogenation of arylchlorosilanes in the presence of catalysts, the directing effect of the $SiCl_3$ group changes due to the formation of an addition compound of the chlorosilane with the catalyzing metal chloride – $ArSiCl_3 \cdot MeCl_3$, as was shown previously with phenyltrichlorosilane [4]. Such a substituent (A) strongly activates the benzene nucleus in substitution reactions, directing the entering groups into position 4 when monosubstituted derivatives are formed, and then into position 2 when disubstituted derivatives are formed.



(A)

Two ortho-directors, located in the 1 and 4 positions, appear in p-tolyltrichlorosilane when it is halogenated in the presence of metal chlorides, in contrast to its halogenation without catalysts described above. This should lead to a considerable general activation of the nucleus, and, in particular, of all four of its unsubstituted hydrogen atoms. This was actually observed – halogenation proceeded very readily even at room temperature and at 20-25° a trichloro derivative of p-tolyltrichlorosilane was formed. As was shown above, under conditions of catalytic halogenation the monosubstituted halogen derivatives of p-tolyltrichlorosilane contained halogen in the ortho-position to the CH_3 group, but even with the dibromo derivative both possible isomers were formed, though with a predominance of the isomer containing both bromine atoms in positions ortho to the CH_3 group.

We consider that the predominant direction of chlorine and bromine into the position ortho to the methyl group is not a result of greater activity of these positions relative to the activity of the other two ortho-positions activated by the $SiCl_3 \cdot MeCl_3$-group. It results rather from the shielding effect of the trichlorosilyl group which leads to a greater reaction rate in the direction observed. This reasoning is in agreement with the order of substitution of hydrogen atoms during halogenation of phenyltrichlorosilane in the presence of catalysts [6] given above. That substitution in the position ortho to the $SiCl_3 \cdot MeCl_3$-group is sterically hindered is, to a certain degree, also confirmed by the fact that, in contrast to trichloro-p-tolyltrichlorosilane, its tribromo analog cannot be prepared and neither can tetrachloro-p-tolyltrichlorosilane; in trying to synthesize these compounds, as described above, by the halogenation of dibromo- or trichloro-p-tolyltrichlorosilane under more drastic temperature conditions, instead of a hydrogen atom being substituted, the C–Si bond was broken.

In this manner, with p-tolyltrichlorosilane also we were able to observe the double nature of the directing effect of the $SiCl_3$ group, which functions as an ortho-, para-director in halogenation in the presence of metal chlorides, and as a meta-director without them.

EXPERIMENTAL

1. Preparation of monochlorotolyltrichlorosilane. Into a mixture of 20.0 g of p-tolyltrichlorosilane[*] (b.p. 103-105° at 15 mm and d_{20}^{20} 1.2835) and 0.1 g of $SbCl_3$ was passed a current of dry chlorine at 22-50° for 1 hour 40 minutes at a rate of 20 ml/min. The increase in weight of the reaction mixture, after passing dry air through it, was 2.9 g (compared with 3.1 g required for chlorination to the monochloro derivative). On distilling the chlorination product in vacuum (15 mm) we obtained the following fractions: 1st, b.p. 105-125°, 1.8 g; 2nd, b.p. 125-140°, 20.7 g. On redistilling the second fraction we obtained 19.5 g of a liquid with b.p. 130-137° at 15 mm, which was monochlorotolyltrichlorosilane. The yield was 84.7%, calculated on the p-tolyltrichlorosilane used in the reaction. Monochlorotolyltrichlorosilane is a colorless, mobile liquid, which fumes in air and has b.p. 132-133° at 15 mm, d_{20}^{20} 1.3948.

Found %: Cl (total)[**] 54.0, 54.3; Cl (hydrolyzable) 41.5, 41.2, $C_7H_6ClSiCl_3$. Calculated %: Cl (total) 54.6; Cl (hydrolyzable) 40.96.

To prove the structure of the monochlorotolyltrichlorosilane it was decomposed with bromine water (2.5 g of the silane, 1.2 ml of bromine and 2.4 ml of water were heated for 7 hours at 180-220° in a sealed tube); from this we isolated a light yellow liquid, which was a chlorobromotoluene (1.4 g, 73% yield). For identification of the chlorobromotoluene it was oxidized with chromic acid ($K_2Cr_2O_7 + H_2SO_4$) and converted into a carboxylic derivative, which was 2-chloro-4-bromobenzoic acid (1.3 g, 81.4% yield) with m.p. 164-165° (from alcohol). Literature data [7]: 2-chloro-4-bromobenzoic acid, m.p. 166-167°; 3-chloro-4-bromobenzoic acid, m.p. 218°. These data showed that the monochlorotolyltrichlorosilane prepared was 3-chloro-4-methylphenyltrichlorosilane.

2. Preparation of dichlorotolyltrichlorosilane. A current of dry chlorine was passed into a mixture of 20.6 g of p-tolyltrichlorosilane and 0.1 g of $SbCl_3$ for 3 hours 20 minutes at a rate of 20 ml/min, keeping the temperature of the reaction mixture at 50° during the first hour of chlorination and then at 65-70° to the end of the reaction. The increase in weight of the reaction mixture after flushing was 6.0 g (compared with 6.2 g required for chlorination to the dichloro derivative). Distillation of the chlorination product in vacuum (15 mm) gave the following fractions: 1st, b.p. 125-140°, 6.0 g; 2nd, b.p. 140-158°, 18.3 g. On redistilling the 2nd fraction we obtained 16.2 g of a liquid with b.p. 150-156° at 15 mm, which was dichlorotolyltrichlorosilane. The dichlorotolyltrichlorosilane was a colorless, mobile, oily liquid, which fumed in air and had b.p. 151-154° at 15 mm, d_{20}^{20} 1.5126.

Found %: Cl (total) 60.10, 60.30; Cl (hydrolyzable) 36.65, 35.97. $C_7H_5Cl_2SiCl_3$. Calculated %: Cl (total) 60.27; Cl (hydrolyzable) 36.16.

The first fraction was monochlorotolyltrichlorosilane. The total yield of the chlorotolyltrichlorosilane was 82.8%.

Considering the data obtained in proving the structure of the dibromotolyltrichlorosilane (see below), it appears that the dichlorotolyltrichlorosilane obtained was a mixture of the 3,5- and 3,6-dichloro isomers.

3. Preparation of trichlorotolyltrichlorosilane. Chlorination of p-tolyltrichlorosilane to the trichloro deriv-

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[*] p-Tolyltrichlorosilane was prepared by treating $p\text{-}CH_3C_6H_4MgBr$ with $SiCl_4$.

[**] "Total" chlorine was determined by the Carius method.

ative was performed under the same conditions as for the dichloro derivative; only the amount of chlorine passed in was appropriately increased.

A current of dry chlorine was passed into a mixture of 20.5 g of p-tolyltrichlorosilane and 0.1 g of $SbCl_3$ for 5 hours 10 minutes at a rate of 20 ml/min, keeping the temperature of the reaction mixture at 50-60° for the first hour of chlorination and then at 70-80° to the end. The increase in weight of the reaction mixture after flushing was 8.8 g (compared with 9.5 g required for chlorination to the trichloro derivative). The chlorination product crystallized as it cooled. On distilling it in vacuum (15 mm) we obtained the following fraction: 1st, b.p. 145-160°, 5.8 g; 2nd, b.p. 160-176°, 22.1 g. On redistilling the 2nd fraction we obtained 20.8 g of a clear (in the hot state) colorless liquid with b.p. 168-172° at 15 mm, which crystallized on cooling to a solid substance – trichlorotolyltrichlorosilane.

Trichlorotolyltrichlorosilane is a white crystalline substance with b.p. 168-172° at 15 mm and readily soluble in acetone. On recrystallization from ether it formed needles with m.p. 44-47°.

Found %: Cl (total) 64.3, 64.12; Cl (hydrolyzable) 32.23, 31.82. $C_7H_4Cl_3SiCl_3$. Calculated %: Cl (total) 64.74; Cl (hydrolyzable) 32.37.

The first fraction was dichlorotolyltrichlorosilane. The total yield of chlorotolyltrichlorosilanes was 89.0%.

The indistinctness of the boiling and melting points of the trichlorotolyltrichlorosilane obtained showed that it was a mixture of isomers.

4. Attempts at the preparation of tetrachlorotolyltrichlorosilane. A current of dry chlorine was passed into a mixture of 20.3 g of p-tolyltrichlorosilane and 0.1 g of $SbCl_3$ for 12 hours at a rate of 20 ml/min at 70-80° for the first four hours and then at 95-100° to the end of the reaction. The increase in weight of the reaction mixture after flushing was 10.4 g. Besides this, in a receiver on the gas outlet of the reactor, surrounded with a cooling mixture (−40°), we obtained 2.6 g of a light yellow liquid with a sharp smell, which was $SiCl_4$. Thus, the total increase in weight of the reaction mixture was 13.0 g (compared with 12.3 g required for chlorination to the tetrachloro derivative). The chlorination product quickly crystallized on cooling. On distilling it in vacuum (15 mm) we isolated a fraction with b.p. 198-215°, 24.2 g, which completely crystallized (m.p. 95-115°) and was only partly soluble in dry acetone on heating. The residue, which was insoluble in acetone, formed crystals (needles) with m.p. 218-219°, and had the smell of polyhalogen derivatives of aromatic hydrocarbons. An attempt at a second fractionation of the fraction isolated did not give positive results as the components of this fraction had close boiling points in vacuum. Therefore, to investigate the composition of this fraction, the latter was dissolved in excess acetone with heating. The insoluble part was filtered off, washed with cold acetone and dried. We obtained white, needle-like crystals (1.0 g), which according to the chlorine content and m.p. 218-219° corresponded to pentachlorotoluene (literature data: pentachlorotoluene m.p. 218°).

Found %: Cl 66.8, 66.9. $C_7H_3Cl_5$. Calculated %: Cl 67.1.

The acetone filtrate was cooled at a temperature of −35 to −40° and the precipitate which formed was filtered off (2.0 g). It had an indistinct m.p. 100-110° and from the analysis on the chlorine content, it was tetrachlorotoluene with some pentachlorotoluene as impurity.

Found %: Cl 62.0, 62.8. $C_7H_4Cl_4$. Calculated %: Cl 61.7. $C_7H_3Cl_5$. Calculated %: Cl 67.1.

After removal of the tetra- and pentachlorotoluenes, the acetone solution was treated with water to convert the chlorotolyltrichlorosilanes in it into a polysiloxane resin. The white, gummy mass formed by diluting the acetone solution with water was extracted with ether and the ether solution was filtered to remove a small amount of insoluble residue. After distilling off the ether and heating the residue, we obtained a clear, light yellow resin (15.8 g), which corresponded to the composition $(CH_3C_6HCl_3SiO_{1.5})_n$ by analysis.

Found %: Cl 42.9, 43.1; Si 10.9, 11.0. $(CH_3C_6HCl_3SiO_{1.5})_n$. Calculated %: Cl 43.2; Si 11.13.

The formation of this resin apparently resulted from hydrolysis of trichlorotolyltrichlorosilane with subsequent condensation of the hydrolysis products.

Thus, the fraction isolated in the vacuum distillation contained a mixture of tetra- and pentachlorotoluenes together with trichlorotolyltrichlorosilane. The yield of trichlorotolyltrichlorosilane, calculated on the amount of resin obtained was 70.7%.

5. Preparation of 3-chloro-4-(chloromethyl)-phenyltrichlorosilane by thermal chlorination of p-tolyltrichlorosilane in the absence of catalysts. 20.0 g of p-tolyltrichlorosilane was chlorinated at 22-25° for 15 hours (chlorine rate of 20 ml/min). The chlorination proceeded without evolution of heat and a lot of chlorine passed through without being absorbed. At the end of the chlorination and flushing no increase in weight of the reaction mixture was detected. Therefore, the chlorination of p-tolyltrichlorosilane was continued at 95-98° for 13 hours. The increase in weight of the reaction mixture after flushing was 2.8 g (compared with 3.1 g required for chlorination to the monochloro derivative). The chlorination proceeded with difficulty and a lot of chlorine passed through without being absorbed. On distilling the chlorination product in vacuum (15 mm) we obtained the following fractions: 1st, b.p. 95-125°, 5.6 g; 2nd, b.p. 125-133°, 6.0 g; 3rd, b.p. 133-138°, 8.0 g. The 1st fraction was unchanged p-tolyltrichlorosilane. On redistilling the 2nd fraction we obtained 4.8 g of a liquid with b.p. 130-133° at 15 mm, d_{20}^{20} 1.4120, which according to its hydrolyzable chlorine content was a mixture of monochlorotolyltrichlorosilane and its chloromethyl derivative.

Found %: Cl (hydrolyzable) 44.6, 44.5. $CH_3C_6H_3ClSiCl_3$. Calculated %: Cl (hydrolyzable) 40.96. $CH_2ClC_6H_3ClSiCl_3$. Calculated %: Cl (hydrolyzable) 48.2.

On redistilling the 3rd fraction we obtained 7.0 g of a liquid with b.p. 135-137° at 15 mm, d_{20}^{20} 1.4645, which was the chloromethyl derivative of monochlorotolyltrichlorosilane.

Found %: Cl (hydrolyzable) 48.0, 48.5. $CH_2ClC_6H_3ClSiCl_3$. Calculated %: Cl (hydrolyzable) 48.2.

The total yield of chlorotolyltrichlorosilane was 51.0%.

To prove the structure of the chloromethyl derivative of monochlorotolyltrichlorosilane it was decomposed with bromine water (2.6 g of the silane, 1.1 ml of bromine and 2.5 ml of water were heated for 7 hours at 180-210° in a sealed tube) with subsequent oxidation of the chlorobromotoluene obtained with chromic acid; from this we isolated a crystalline substance with m.p. 166°, which was 2-chloro-4-bromobenzoic acid. These data show that the chloromethyl derivative obtained was 3-chloro-4-(chloromethyl)-phenyltrichlorosilane.

6. Preparation of monobromotolyltrichlorosilane. Over a period of 20 minutes, 17.5 g of dry bromine was added dropwise at room temperature to a mixture of 22.2 g of p-tolyltrichlorosilane and 0.1 g of metallic iron powder. After the addition of all the bromine the reaction mixture was heated for 20 minutes at 60° to complete the reaction, after which it was flushed with dry air to remove the residual hydrogen bromide. The increase in weight of the reaction mixture after flushing was 8.0 g (compared with 7.7 g required for bromination to the monobromo derivative). Distillation of the bromination product in vacuum (10 mm) gave the following fractions: 1st, b.p. 95-125°, 1.0 g; 2nd, b.p. 125-142°, 26.0 g. On redistilling the 2nd fraction we obtained 24.0 g of a colorless liquid with b.p. 136-137° at 10 mm, which was monobromotolyltrichlorosilane. The yield was 80.2%, calculated on the p-tolyltrichlorosilane taken for the reaction.

Monobromotolyltrichlorosilane is a colorless, mobile, oily liquid, which fumes in air and slowly crystallizes on standing (plates), b.p. 136-137° at 10 mm, d_{20}^{20} 1.6320.

Found %: Cl (hydrolyzable) 34.47, 34.56. $C_7H_6BrSiCl_3$. Calculated %: Cl (hydrolyzable) 34.97.

To determine the bromine content, a small part of the monobromotolyltrichlorosilane obtained was treated with water and converted to a resin, which was analyzed for bromine.

Found %: Br 35.81, 35.92. $(CH_3C_6H_3BrSiO_{1.5})_n$. Calculated %: Br 36.03.

To prove the structure of the monobromotolyltrichlorosilane it was decomposed with bromine water (8.7 g of silane, 2.3 ml of bromine and 5.0 ml of water were heated for 8 hours at 180-240° in a sealed tube). After the heating the tube was opened and its contents were treated as in the decomposition of chlorophenyltrichlorosilanes. As a result we isolated a liquid (5.4 g, 76.0% yield) with b.p. 236-240°, which did not solidify on cooling and corresponded to dibromotoluene according to analysis for bromine content.

Found %: Br 64.4, 64.3. $C_7H_6Br_2$. Calculated %: Br 64.0.

To identify the dibromotoluene obtained, the latter was oxidized with 20% nitric acid and converted into a dibromobenzoic acid. A mixture of 1.2 g of dibromotoluene and 2.5 ml of 20% HNO_3 was heated at 180-200° for 7 hours. The precipitate of dibromobenzoic acid formed was extracted with ether and for purification, it was converted into the sodium salt by dissolving 10% NaOH with subsequent liberation of the free acid by neutralization of the solution with 10% H_2SO_4 solution.

The crystalline substance obtained (1.1 g, 88% yield) corresponded to a dibromobenzoic acid according to bromine content.

Found %: Br 56.7, 56.9. $C_7H_4O_2Br_2$. Calculated %: Br 57.14.

The melting point of the dibromobenzoic acid (171-173°) indicated that it was the 2,4-dibromo isomer. Literature data: 2,4-dibromobenzoic acid, m.p. 168-169°, 172-173° [8], 3,4-dibromobenzoic acid, m.p. 228°, 232-233° [9]. A mixed m.p. of the crystals obtained with synthetic 2,4-dibromobenzoic acid was not depressed on melting. From these data it follows that the monobromotolyltrichlorosilane obtained was the 3-bromo isomer.

7. Preparation of dibromotolyltrichlorosilane. The bromination of p-tolyltrichlorosilane to the dibromo derivative was performed under similar conditions, only with an increase in the amount of bromine used in the reaction. Over a period of 1 hour 50 minutes, 33.0 g of bromine was added dropwise with stirring at 25-40° to a mixture of 21.2 g of p-tolyltrichlorosilane and 0.1 g of metallic iron powder, after which the reaction mixture was heated for 0.5 hours at 60-70° to complete the reaction. The increase in weight of the reaction mixture after flushing was 15.0 g (compared with 14.8 g required for bromination to the dibromo derivative). The bromination product crystallized as it cooled. On distilling it in vacuum (10 mm) we obtained the following fractions: 1st, b.p. 125-140°, 4.0 g; 2nd, b.p. 140-165°, 30.2 g. On redistilling the 2nd fraction we obtained 28.1 g of a colorless liquid (in the hot state), which crystallized on cooling and was dibromotolyltrichlorosilane with b.p. 163-166° at 10 mm.

Dibromotolyltrichlorosilane is a white crystalline substance with b.p. 163-166° at 10 mm, m.p. 56-63° (from ether).

Found %: Cl (hydrolyzable) 27.4, 27.55. $C_7H_5Br_2SiCl_3$. Calculated %: Cl (hydrolyzable) 27.77.

To determine the bromine content, part of the dibromotolyltrichlorosilane obtained was converted into a polysiloxane resin, which was analyzed for bromine.

Found %: Br 52.79, 52.86. $(CH_3C_6H_2Br_2SiO_{1.5})_n$. Calculated %: Br 53.15.

The 1st fraction was mainly monobromotolyltrichlorosilane. The total yield of bromotolyltrichlorosilanes was 91.4%.

To prove the structure of dibromotolyltrichlorosilane it was decomposed with bromine water (5.5 g of the silane, 1.3 ml of bromine and 3.5 ml of water were heated for 8 hours at 180-240° in a sealed tube). From the reaction products we isolated a crystalline substance (3.3 g, 71.2% yield), as needles (from alcohol) with m.p. 67-82°, which corresponded to a tribromotoluene according to bromine content.

Found %: Br 72.9, 72.5. $C_7H_5Br_3$. Calculated %: Br 72.6.

The extended melting point of the tribromotoluene obtained indicated that it was a mixture of several isomers (according to literature data: melting points for 2,4,6-, 2,3,4-, 2,4,5- and 3,4,5-tribromotoluenes are respectively equal to 65-66°, 44-46°, 112-113.5° and 88-91°).

Taking into account the structure of the monobromotolyltrichlorosilane (see above), on the one hand, and the melting point of the tribromotoluene isolated, on the other, one can assume that the latter is a mixture of

2,4,6- and 2,4,5-tribromotoluenes with a predominance of the first isomer. From these data it follows that the dibromotolyltrichlorosilane obtained is a mixture of the 3,5- and 3,6-dibromo isomers, containing a larger amount of the first isomer. The extended melting and boiling points of the dibromotolyltrichlorosilane synthesized also indicates a mixture of isomers.

8. Attempts at the preparation of tribromotolyltrichlorosilane. 48 g of dry bromine was added dropwise with stirring to a mixture of 20.0 g of p-tolyltrichlorosilane and 0.1 g of metallic iron powder (p-$CH_3C_6H_4SiCl_3 : Br_2 = 1:3.4$). The first 2/3 of the bromine was added over a period of 2 hours at 25-40°, when practically the whole of the bromine reacted. Since further absorption of bromine proceeded with difficulty, the last 1/3 of it was added over a period of 1.5 hours at 80-90°. After adding all the bromine, the reaction mixture was heated for 1.5 hours at 90-95° to complete the reaction. The bromination product crystallized on cooling. The increase in weight of the reaction mixture after flushing was 16.9 g (compared with 21.0 g required for bromination to the tribromo derivative). Besides this, in the receiver on the gas outlet of the reactor, surrounded with a cooling mixture (−40°), we obtained 8.6 g of a dark orange liquid with a sharp smell, which was $SiCl_3Br$ (b.p. 79-80°, not crystallizing at −60°). On distilling the bromination product in vacuum (10 mm) we isolated a fraction with b.p. 163-185°, 32.9 g, which completely crystallized. This fraction was investigated in the same way as described above in the attempts to prepare tetrachlorotolyltrichlorosilane. The residue insoluble in excess acetone (~4.0 g) was a white, crystalline substance, needles, with m.p. 150-180°, which corresponded to a mixture of tetra- and pentabromotoluene according to the bromine content (literature data: 2,3,4,6-tetrabromotoluene, m.p. 105-108°, 2,3,4,5-tetrabromotoluene, m.p. 111-115°; pentabromotoluene, m.p. 279-280°).

Found %: Br 80.1, 80.4. $C_7H_4Br_4$. Calculated %: Br 78.4. $C_7H_3Br_5$. Calculated %: Br 82.1.

Crystals isolated from the acetone solution after cooling it to from −40 to −50° (11.2 g), corresponded in bromine analysis to tetrabromotoluene, containing tribromotoluene as a slight impurity.

Found %: Br 77.2, 77.6. $C_7H_5Br_3$. Calculated %: Br 73.0. $C_7H_4Br_4$. Calculated %: Br 78.4.

The extended melting point of the crystals isolated (100-115°) also indicated the presence of a mixture of tri- and tetrabromotoluenes. Literature data: 2,4,6-tribromotoluene, m.p. 65-66°, 2,4,5-tribromotoluene, m.p. 112-113.5°.

After the removal of the bromotoluene, the acetone solution was treated with water and steam distilled (to remove residual bromotoluenes). The residue after distillation was a clear, light yellow resin (12.6 g), which from analysis for bromine and silicon contents corresponded to the composition $(CH_3C_6H_2Br_2SiO_{1.5})_n$.

Found %: Br 53.4, 53.6; Si 9.4, 9.6. $(CH_3C_6H_2Br_2SiO_{1.5})_n$. Calculated %: Br 53.1; Si 9.3.

The formation of this resin apparently resulted from hydrolysis of the dibromotolyltrichlorosilane with subsequent condensation of the hydrolysis products.

Thus, the fraction isolated in the vacuum distillation contained a mixture of tri-, tetra- and pentabromotoluenes together with dibromotolyltrichlorosilane. The yield of dibromotolyltrichlorosilane, calculated on the amount of resin obtained, was 47.4%.

9. Preparation of 3-bromo-4-(bromomethyl)-phenyltrichlorosilane by thermal bromination of p-tolyltrichlorosilane in the absence of catalysts. Over a period of 1.5 hours 13.6 g of dry bromine was added dropwise to 19.2 g of p-tolyltrichlorosilane and the mixture kept for 12.5 hours at 90-95°. The increase in weight of the reaction mixture after flushing was 5.5 g (compared with 6.6 g required for bromination to the monobromo derivative). Distillation of the bromination product in vacuum (10 mm) gave the following fractions: 1st, b.p. 103-145°, 6.0 g; 2nd, b.p. 145-150°, 18.0 g. The 1st fraction was mainly unchanged p-tolyltrichlorosilane. On redistilling the 2nd fraction we obtained 16.0 g of a liquid with b.p. 148-150° at 10 mm, d_{20}^{20} 1.6353, which was the bromomethyl derivative of monobromotolyltrichlorosilane.

Found %: Cl + Br (hydrolyzable) 47.9, 48.2. $BrCH_2C_6H_3BrSiCl_3$. Calculated %: Cl + Br (hydrolyzable) 48.5.

The total yield of bromotolyltrichlorosilanes was 52.0%.

The structure of the bromomethyl derivative of monobromotolyltrichlorosilane was proved by a method similar to that for the chloromethyl derivative (see above). From the products of decomposition and oxidation we isolated 2,4-dibromobenzoic acid (m.p. 170-171°), indicating that the bromomethyl derivative of monobromotolyltrichlorosilane was 3-bromo-4-(bromomethyl)-phenyltrichlorosilane).

Experiments on the chlorination of p-tolyltrichlorosilane in the presence of metallic iron, reported in Table 1, were carried out by a method similar to that for the chlorination of p-tolyltrichlorosilane in the presence of $SbCl_3$.

SUMMARY

1. Chlorination of p-tolyltrichlorosilane in the presence of the usual catalysts for halogenation of aromatic compounds (iron, $SbCl_3$) may give mono-, di- and trichloro derivatives. Bromination of p-tolyltrichlorosilane under these conditions gave mono- and dibromo derivatives. We did not succeed in preparing tetrachloro and tribromo derivatives of p-tolyltrichlorosilane, substituted in the nucleus.

2. It was established that chlorination and bromination of p-tolyltrichlorosilane in the presence of a catalyst was accompanied by destructive halogenation, due to cleavage of the silane molecule at the C–Si bond. This side reaction occurs more readily in p-tolyltrichlorosilane than in phenyltrichlorosilane.

3. It was found that only in the case of chlorination and bromination of p-tolyltrichlorosilane to the monohalo derivative were discrete compounds formed, namely 3-chloro(bromo)-4-methylphenyltrichlorosilanes. With further halogenation, mixtures of isomers of di- and trihalo derivatives were formed.

4. It was shown that in substitution reactions in the nucleus, p-tolyltrichlorosilane behaved normally in the absence of catalysts. In halogenation of p-tolyltrichlorosilane under these conditions, the halogen atom entering the nucleus, was directed by both substituents ($1-CH_3$, $4-SiCl_3$), in accordance with their nature, to position 2.

5. In halogenation of p-tolyltrichlorosilane in the presence of catalysts, the halogen atom was mainly directed into the position ortho to the CH_3 group and not ortho to the $SiCl_3$ group, as was to be expected in analogy to phenyltrichlorosilane, and this, apparently, is the result of the shielding effect of the trichlorosilane group.

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THE REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

V. REACTIONS OF DIAZO COMPOUNDS WITH N-PHENYLSULFAMIC ACID

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We showed in a previous report [1] that the expected aryltriazene-N-sulfonates $ArN{=}N{-}NH{-}SO_3Na$ were not obtained by treating a salt of unsubstituted sulfamic acid with diazo compounds. Assuming that the reason for this was the instability of aryltriazene-N-sulfonates due to the presence of hydrogen in them that was capable of exchange, we investigated the reaction of diazo compounds with N-methylsulfamic acid and showed that it gave quite stable aryl-1-methyl-3-triazenesulfonates-3 $ArN{=}N{-}N(CH_3)SO_3Na$, which were the N-sulfo acids of aliphatic-aromatic triazenes.

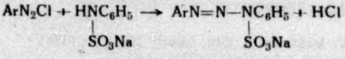
In the present work we investigated the reaction of diazo compounds with N-phenylsulfamic acid, as the simplest example of the arylsulfamic acid series, with the purpose of preparing diaryltriazene-N-sulfonates $Ar{-}N{=}N{-}N(Ar')SO_3Na$.

It was found that the reaction of diazo compounds with sodium phenylsulfamate in acidic media (pH from 2 to 5) gave strongly colored phenylsulfamate salts of diazo compounds by the reaction

$$ArN_2Cl + C_6H_5NHSO_3Na \longrightarrow ArN_2OSO_2NHC_6H_5 + NaCl$$

Our next paper will be devoted to the description of the synthesis and properties of these interesting diazo salts.

Diazoamino condensation occurred in the reaction of diazo compounds with sodium phenylsulfamate in media with pH from 4 to 7, according to the following scheme

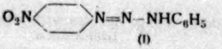


$$ArN_2Cl + \underset{\displaystyle SO_3Na}{HNC_6H_5} \longrightarrow ArN{=}N{-}\underset{\displaystyle SO_3Na}{NC_6H_5} + HCl$$

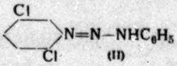
The course of the reaction is characterized by the gradual disappearance of a reaction for an active diazo group and the separation of hydrochloric acid, which must be removed by the addition of bicarbonate or treatment with a strong buffer.

However, after completion of the diazoamino condensation, we were unable to isolate from the reaction suspension, the expected diaryltriazene-N-sulfo acids which should have had a definite solubility in water. Instead of them, mixed, water-insoluble triazenes of the type $ArN{=}N{-}NHC_6H_5$.

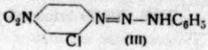
For example, the reaction of sodium phenylsulfamate with 4-nitrophenyldiazonium gave 4-nitrophenyltriazene (I), with 2,5-dichlorophenyldiazonium – 2,5-dichlorodiphenyltriazene (II) and with 4-nitro-2-chlorophenyldiazonium – 4-nitro-2-chlorodiphenyltriazene (III).



(I)



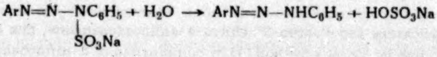
(II)



(III)

To identify the triazenes obtained, we synthesized the known triazenes (I), (II) and (III) by condensing the appropriate diazo compounds with aniline in an acetate medium [2]. The last two of these triazenes were synthesized for the first time. The triazenes specially synthesized were found to be identical in their physical and chemical properties with those isolated from the reaction of the corresponding diazo compounds with phenylsulfamic acid.

The formation of unsymmetrical diaryltriazenes as the main reaction products of diazo compounds and sodium phenylsulfamate may be explained only by hydrolytic cleavage of the sulfo group from the diaryltriazene-N-sulfonates that were formed initially.



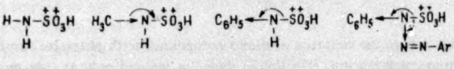
$$ArN{=}N{-}\underset{\displaystyle SO_3Na}{N}C_6H_5 + H_2O \longrightarrow ArN{=}N{-}NHC_6H_5 + HOSO_3Na$$

Actually, sulfuric acid (~50% of the theoretical amount) was detected in the filtrates from the precipitates formed during the condensation of diazo compounds with phenylsulfamic acid.

It was thus established that even at pH 5-6, which is the optimal for diazoamino condensation, diaryltriazene-N-sulfonates are capable of splitting off their sulfo group. Consequently, the sulfo group is bonded to nitrogen in these compounds much more labilely than in the 1,3-methylaryltriazene-N-sulfonates that we synthesized earlier [3]. This can be readily explained by the following reasoning. The unsubstituted sulfamic acid contains a sulfo group which is quite unstable bound to the amino group. It is stable in an aqueous solution at room temperature, but splits off its sulfo group, forming ammonium bisulfate, at higher temperatures [4].

$$NH_2SO_3H + H_2O \longrightarrow NH_3 + HOSO_3H \longrightarrow NH_4HSO_4$$

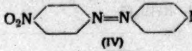
Alkylsulfamic acids and, in particular, methylsulfamic acid, were found to be considerably more stable to hydrolysis as they withstand boiling in an acidic medium, though not for long [5]. The arylsulfamic acids are so unstable that the majority of them are only capable of existing in aqueous solution in the form of their salts [6]. It follows from this that N-aryl-N-azoarylsulfamic acids must be even less capable of retaining their sulfo group even in the salt form. Actually, in a sulfamic acid, the bond between the nitrogen of the amino group and the sulfur of the sulfo group would be strengthened by any electron donor group introduced into the amino group, and would be weakened by an electron acceptor.



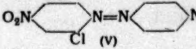
The series given is an interesting illustration of the capacity of a covalent bond between atoms to gradually polarize until it is converted into an electrovalent one, which is dissociated in water, as a result of the effect of groups with increasing electrophilic properties, that are connected to one of the atoms.

Further investigation of the reaction between phenylsulfamic acid and diazo compounds showed that, besides the unsymmetrical diaryltriazenes, products of combination of diazo compounds with phenylsulfamic acid in the position para to the sulfamino group are formed although in a much smaller amount.

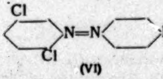
The following N-sulfo derivatives of 4-aminoazobenzene were isolated


reddish-orange needles with a bronze iridescence,

(IV)

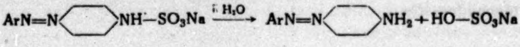

brick-red prisms,

(V)


yellowish-brown crystals.

(VI)

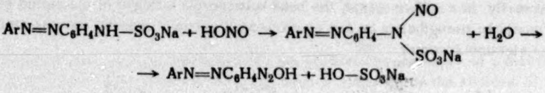
These substances were found to be quite soluble in water, especially when heated, and were of an intensely reddish orange or reddish brown color. They were readily salted out of aqueous solutions by the addition of sodium chloride. Heating their acidified solutions resulted in cleavage of the sulfo group and the separation of 4-aminoazobenzene derivatives, which were insoluble in water.



The 4-nitro-4-aminoazobenzene and 4'-nitro-2'-chloro-4-aminoazobenzene, thus isolated, were identical with the products synthesized: first by Meyer's method [7] by combination of 4-nitrophenyldiazonium chloride with aniline hydrochloride in an acidic medium, and secondly, by the combination of 4-nitro-2-chlorophenyldiazonium with the formaldehyde bisulfite derivative of aniline [8, 9] and splitting off the formaldehyde bisulfite residue from the azo dye obtained with boiling 10% acetic acid. Of these, 4'-nitro-2'-chloro-4-aminoazobenzene, which forms dark red prisms with m.p. 180°, has not been described in the literature previously.

The N-sulfo derivatives of 4-aminoazobenzene are decolorized by hydrosulfite in an alkaline medium and by stannous chloride in hydrochloric acid, forming, in the latter case, p-phenylendiamine without the slightest trace of o- and m-phenylendiamines. Consequently, combination occurs exclusively at the position para to the sulfamino group, as has already been observed by other authors in the combination of diazo compounds with α-naphthylsulfamic acid [10]. It was noted that the combination of diazo compounds with aniline hydrochloride, by Meyer's method, in an acidic medium resulted in impure products from which pure 4-aminoazobenzene derivatives may be isolated only after many recrystallizations from various solvents. From this, one may assume that under these conditions, the diazo residue enters the aniline molecule not only at the position para to the amino group.

N-sulfoaminoazo dyes, as with arylsulfamic acids [11], are, apparently first nitrosated when treated with nitrite in an acidic medium, and then the labile sulfo group is split off and a diazo compound is formed.



$$\mathrm{ArN{=}NC_6H_4NH{-}SO_3Na + HONO \longrightarrow ArN{=}NC_6H_4{-}N}\begin{matrix}\diagup \mathrm{NO}\\ \diagdown \mathrm{SO_3Na}\end{matrix} + \mathrm{H_2O} \longrightarrow$$

$$\longrightarrow \mathrm{ArN{=}NC_6H_4N_2OH + HO{-}SO_3Na}$$

It is interesting to note that in the reaction of diazo compounds with phenylsulfamic acid at pH values of 5-6.5, optimal for diazoamino condensation, N-sulfoazo dyes are formed only as side products, in a yield of the order of 3-6%. However, if the reaction is carried out at pH 4-4.5, the yield of N-sulfoaminoazo dyes is 20-40%. Consequently, the azo combination of phenylsulfamic acid is promoted by a medium more acidic than that for diazoamino condensation.

Even so, phenylsulfamic acid has a much lower capacity for azo combination than α-naphthylsulfamic acid. As is known, the same difference in capacity for azo combination exists, between aniline and α-naphthylamine, due to the high reactivity of the para-carbon in α-naphthylamine.

EXPERIMENTAL

Synthesis of starting materials. Sodium phenylsulfamate was prepared by sulfonating aniline with chlorosulfonic acid in pyridine and neutralizing the sulfonation product with soda as described for phenylenediamines [12]. The sodium phenylsulfamate obtained after distilling off the pyridine and evaporating down the solution, was purified by extraction with alcohol and recrystallized from boiling alcohol. Analysis with nitrite showed that the recrystallized product contained 99.2% of the pure substance.

Solutions of the diazo compounds were prepared by stirring for half an hour 0.01 mole of the amine with 0.03-0.05 mole of 5 N hydrochloric acid, adding 7 g of crushed ice and pouring in 2.1 ml of 5 N sodium nitrite solution in one portion. The solution obtained was filtered and the excess nitrous acid removed by adding several drops of sulfamic acid solution, using paper soaked in metanil yellow solution as indicator.

Treatment of 4-nitrodiazobenzene with phenylsulfamic acid. 0.033 mole of sodium phenylsulfamate was dissolved in 50 ml of water, 45 ml of concentrated acetate buffer at pH 6 added, the solution cooled to −3° and a cold solution of 0.03 mole of 4-nitrodiazobenzene added to it with vigorous stirring. Brownish-red crystals of the diazonium salt of phenylsulfamic acid immediately separated from the solution. With further stirring these crystals disappeared and in their place a fine, considerably lighter precipitate appeared. During the diazoamino condensation free hydrochloric acid was liberated and sulfuric acid was hydrolytically split out of the unstable diazoamino compound. Therefore, to maintain the pH of the reaction mixture at about 6 a solution of sodium bicarbonate was added dropwise. The suspension gradually became brownish-yellow.

Testing the reaction mixture for active diazo compounds with H-acid at first gave an intense violet color on filter paper and after 5 hours stirring at a temperature, which was gradually raised to room, it gave a pale pink, which increased to cherry on leaving the paper in air. When the reaction for active diazo compound had weakened, the suspension was cooled with ice and filtered. The precipitate was pressed out and dried in a desiccator. Its color was brownish-yellow and the weight 11.2 g.

Investigation of the precipitate. a) The product insoluble in water. The precipitate was twice extracted with water, heated to 85°, filtered off, washed with hot water and dried at 75°. Its weight was 6.7 g. Then the precipitate was repeatedly crystallized from alcohol, ligroin and benzene. As a result of this the melting point rose from 135-137° after the first recrystallization to 147° after the last.

On dissolving the product isolated in glacial acetic acid, adding a few crystals of α-naphthylamine and heating, an intense cherry-red color appeared, which is characteristic for diaryltriazenes that are insoluble in water [13]. A color reaction on the diazoamino compound could also be obtained if the product was suspended in concentrated hydrochloric acid, slightly heated and a few drops of a suspension of H-acid in soda solution added.

On adding potassium hydroxide to a suspension of the substance investigated in water and heating, it gave an intense red color, which disappeared on neutralizing with free alkali. On boiling the substance with soda solution, it gave a less bright color, which disappeared on cooling. These properties are characteristic of nitrodiaryltriazenes [14].

For identification we synthesized 4-nitrodiazoaminobenzene by diazoamino condensation of 4-nitrodiazobenzene with aniline [2]. After two recrystallizations from alcohol, the product obtained gave yellow crystals, which appeared as needles under a microscope and had m.p. 146.0° on gradual heating and 147.5° on putting the capillary into sulfuric acid heated to 130°. A mixed melting point of the authentic 4-nitrodiphenyltriazene with the substance obtained in the condensation of 4-nitrodiazobenzene with phenylsulfamic acid was not depressed. Color reactions with solutions of α-naphthylamine in acetic acid and with solutions of potassium hydroxide and soda also were completely identical for the authentic triazene and that investigated.

b) The product soluble in water. The hot water, used to extract the precipitate obtained in the condensation of 4-nitrodiazobenzene with phenylsulfamic acid, had an intense orange-red color and on cooling in ice, a flocculent precipitate separated. After filtering, washing and drying, its weight was 0.31 g (3%). If the condensation of phenylsulfamic acid with 4-nitrodiazobenzene was carried out at a lower pH, for example 4-5, then the reaction for active diazo compound weakened only after 2 days; here the amount of product soluble in water increased to 2.0-2.5 g, which amounted to 20-25%, calculated on the N-sulfaminoazo dye. In the extraction of the azo dye from the reaction precipitate with hot water, the pH had to be not less than 7 to avoid hydrolytic decomposition of the triazene. After one recrystallization of the soluble product from water, we obtained red-orange crystals with a bronze iridescence, which appeared as needles under a microscope. We found nitrogen and sulfur in the substance by fusion with metallic sodium; it did not show reactions for an active or passive diazocompound. The intense color of the aqueous solution and the ready salting out of a precipitate from it by electrolytes indicated that the substance investigated was an azo dye containing a sulfo group imparting solubility to it. Actually, an aqueous solution of the dye was readily decolorized on heating with hydrosulfite in an alkaline medium and in hydrochloric acid with stannous chloride. On adding a few crystals of aniline hydrochloride and ferric chloride to the solution, decolorized with stannous chloride, it gave an intense blue-green color and after standing for a short time – a blue precipitate of indamine, characteristic of p-phenylenediamine [15]. Qualitative reactions for o- and m-phenylenediamines gave negative results. From this, it was assumed that the substance investigated was a sulfonated azo dye with the following structure: p-$O_2N-C_6H_4-N=N-C_6H_4-NH_2$ p-.

The position of the sulfo group was established by the following reactions: on acidifying a saturated aqueous solution of the azo dye with hydrochloric acid in the cold a precipitate separated, which was, apparently, the free sulfonic acid of the azo product and which dissolved on gentle heating. On raising the temperature to 80-85° the solution gelled due to the splitting out of the sulfo group from the azo dye forming a gel, which dissolved on further heating giving an orange-pink color. On cooling the solution the pink color disappeared and a copious, light flocculent, red-violet precipitate formed – a mixture of the aminoazo dye, with the sulfo group split out, and its hydrochloride. On washing with water on a filter, this precipitate changed from violet to red due to hydrolytic removal of the molecule of hydrochloric acid forming the salt. After one recrystallization from 40% alcohol we obtained a product with m.p. 216.5-217.0°.

To identify the product obtained we synthesized 4-amino-4'-nitroazobenzene by combining p-nitrophenyldiazonium with aniline hydrochloride in an acid medium [7]. The precipitate formed after 2 hours stirring melted at 211.5-212.5° after drying and recrystallizing from alcohol. After several recrystallizations first from alcohol and then from toluene, we obtained an aminoazo dye with m.p. 215.5-216°, which melted at 215-216° when mixed with our product. With 5 N hydrochloric acid both products formed a blue hydrochloride with a steel shade which was hydrolyzed on adding water. On acidifying with concentrated hydrochloric acid and treating with nitrite, both products formed diazo compounds, which combined with P-salt to give a cherry-colored diazo dye. Consequently, after splitting out the sulfo group, the product investigated had the structure of 4-amino-4'-nitroazobenzene, indicating that the sulfo group was attached not to the nucleus, but to the amino group, which explained the ease of its hydrolysis.

Analysis of the N-sulfazo dye for sulfur content. 0.0958 g of the substance was boiled in 10 ml of water and 1 ml of concentrated hydrochloric acid. The precipitate of 4-amino-4'-nitroazobenzene was filtered off and washed with water. The filtrate and washing water was heated to boiling and $BaCl_2$ added. After drying, the $BaSO_4$ precipitate weighed 0.0645 g.

Found %: S 9.24. $C_{12}H_9O_5N_4SNa$. Calculated %: S 9.32.

c) Investigation of the filtrate. The filtrate from the precipitate, formed by the diazoamino condensation of 4-nitrodiazobenzene with phenylsulfamic acid at pH 6-7, was acidified with hydrochloric acid and treated with barium chloride to precipitate barium sulfate. The weight of the latter for the experiment with 0.03 mole of phenylsulfamic acid and 4-nitrodiazobenzene was 3.2065 g, which amounted to ~45.8%, if we consider that the sole reaction product was 4-nitrodiphenyltriazene.

Treatment of 4-nitro-2-chlorodiazobenzene with phenylsulfamic acid. A solution of 0.01 mole of 4-nitro-2-chlorodiazobenzene in 20 ml of water was added at 16° with stirring to a solution of 0.01 mole of sodium phenylsulfamate in 30 ml of concentrated acetate buffer (pH 4.6). The reaction solution immediately darkened and formed a dark-brown precipitate with a violet tinge of 4-nitro-2-chlorophenyldiazonium-phenylsulfamate. With further stirring the reaction suspension changed from dark-brown to a brick color and the reaction for active diazo compound with H-acid gradually weakened. After 3 hours the precipitate was filtered off, washed with cold water till there was a negative reaction for active diazo compound and pressed out. The weight of the moist precipitate was 4.2 g. A third of the filtrate was treated with barium chloride. We obtained 0.4139 g of $BaSO_4$, which corresponded to 53.2%, calculated on the phenylsulfamic acid.

Investigation of the precipitate. a) The part soluble in water. The precipitate was twice extracted with 25 ml portions of water at 85-90°. The hot filtrates, which had an intense orange-red color, deposited brownish-red crystals (prisms under a microscope) on cooling, which were dried in a thermostat at 50-55°. Their weight was 0.27 g. If the condensation of 4-nitro-2-chlorodiazobenzene with phenylsulfamic acid was carried out at pH 4 at room temperature over a period of two days, the yield of the substance soluble in water increased to 1.15 g, i.e., to ~30%, calculated on the N-sulfaminoazo dye.

The crystals of the N-sulfaminoazo dye were slightly soluble in water in the cold and much more soluble on heating. They could be recrystallized from water and better still from 50% alcohol.

On heating a solution of the crystals with hydrochloric acid and barium chloride a precipitate of barium sulfate formed, which showed that the sulfo group was readily split out from the substance investigated. On heating a solution of the crystals with hydrochloric acid and then treating with nitrite in the cold, a diazo compound was obtained, which combined with any azo component to give an azo dye. Consequently, the substance contained an amino group.

The water-soluble substance investigated was decolorized by an alkaline solution of hydrosulfite or a hydrochloric acid solution of stannous chloride. The solution obtained in the latter case gave a strong indamine reaction for p-phenylenediamine and did not show the presence of o- and m-phenylenediamines. This meant that the product was a p-aminoazo dye.

From the reactions described it was assumed that the substance soluble in water was an N-sulfo derivative of 4-nitro-2-chloro-4'-aminoazobenzene (V).

To confirm this, we synthesized 4-nitro-2-chloro-4'-aminoazobenzene by the following method. The formaldehyde bisulfite derivative was prepared by Bucherer and Schwalbe's method [8]. 5.23 g of this substance was dissolved in 25 ml of water, 20 ml of saturated sodium acetate solution added, the solution cooled to 0° and a further 25 g of ice added. A cold solution of 0.025 mole of 4-nitro-2-chlorophenyldiazonium was added to the solution with stirring. After 40 minutes we filtered off the violet-brown precipitate of the formaldehyde bisulfite derivative of 4-amino-4'-nitro-2'-chloroazobenzene.

An attempt to hydrolyze off the formaldehyde bisulfite residue by heating the dye in 3% sodium hydroxide solution, as described for the similar product from 4-nitrodiazobenzene [9], did not succeed as this apparently led to hydrolysis of the 2'-chloro group. The reaction was accomplished, however, by boiling the substance for 3 hours in 12% acetic acid. After filtering off, washing and drying, the dark precipitate formed was recrystallized first from benzine with b.p. 100-120° and then twice from benzene. The dark-red prismatic crystals of 4-amino-2'-chloro-4'-nitroazobenzene obtained melted at 179-180°.

The N-sulfoaminoazo dye, synthesized by combining 4-nitro-2-chlorodiazobenzene with phenylsulfamic acid and recrystallized, was heated for 5 minutes in water acidified with hydrochloric acid. The precipitate formed was filtered off, washed, dried and recrystallized from an alcohol-benzene mixture. The dark-red crystals obtained appeared as plates under a microscope. Their m.p. was 180-181°. A mixture of the aminoazo dyes, synthesized by both methods, melted at 179-181°, indicating their identity.

The final confirmation of the correctness of the structure proposed for the N-sulfoazo dye was given by its analysis for sulfur and sodium content.

Found %: S 8.28; Na 6.22. $C_{12}H_8O_5N_4SClNa$. Calculated %: S 8.46; Na 6.07.

b) The part insoluble in water. The precipitate obtained in the treatment of 4-nitro-2-chlorodiazobenzene with phenylsulfamic acid and extracted with water, was dried and recrystallized first from alcohol and then from a light benzine. The lustrous brown crystals obtained melted at 119-120° and showed reactions characteristic of nitrodiaryltriazenes: in alcoholic alkali they dissolve with an intense red color and in glacial acetic acid, they combine on heating with α-naphthylamine to give an azo dye with an intense cherry color.

To identify the diaryltriazene obtained, we specially synthesized 4-nitro-2-chlorodiphenyltriazene, which is not described in the literature, by combining 4-nitro-2-chlorodiazobenzene with aniline in an aqueous alcohol solution in the presence of sodium acetate. The precipitate formed by this reaction was dried at 50-60° and after two recrystallizations from benzine, it gave lustrous, light-brown crystals with a reddish tinge, which appeared as prisms under a microscope. Their m.p. was 119.5-120°. The authentic 4-nitro-2-chlorodiphenyltriazene gave color reactions which were completely the same as those of the substance investigated and a mixture of the two products showed no depression in melting point, which definitely confirmed their identity.

Treatment of 2,5-dichlorodiazobenzene with phenylsulfamic acid. 0.02 moles of 2,5-dichloroaniline was dissolved in 0.06 mole of concentrated hydrochloric acid and 20 ml of water, cooled and diazotized with a slight excess of nitrite. The diazo solution was freed from excess nitrous acid by adding sulfamic acid, the mineral acid disposed of by adding sodium acetate and it was poured with stirring into a solution of 0.02 mole of sodium phenylsulfamate in 60 ml of acetate buffer with pH 6.

The reaction solution immediately acquired a red-orange color and began to deposit a precipitate of the same color, which proved to be the 2,5-dichlorophenyldiazonium salt of phenylsulfamic acid. Stirring was continued for 5 hours until the diazonium salt disappeared, which was indicated by the reaction solution changing to a yellow-orange color. However, the reaction for active diazo compound disappeared only after 3 days.

The precipitate was filtered off from the reaction mixture and extracted with hot water containing a small amount of bicarbonate to remove the material soluble in water. After cooling, the filtrate precipitated only 0.15-0.20 g of N-sulfoaminoazo dye, which amounted to 3-4%.

a) The product insoluble in water. The precipitate, freed from the water soluble part, was recrystallized several times from petroleum ether after drying. The coarse, orange crystals obtained had m.p. 85-86°. On dissolving them in glacial acetic acid, containing α-naphthylamine, they gave a cherry-red color.

To identify the diaryltriazene obtained, we synthesized 2,5-dichlorodiphenyltriazene, which is not described in the literature. 20 ml of a saturated sodium acetate solution was added to 1 g of aniline in 1 ml of alcohol, the solution cooled to 0° and 0.01 mole of 2,5-dichlorophenyldiazonium was added dropwise with vigorous stirring. After several minutes the reaction vessel was full of an orange precipitate and the reaction for active diazo compound disappeared. After filtering, washing, pressing out and drying in a vacuum desiccator over potassium hydroxide, the precipitate weighed 2.0 g, which was 75%. After recrystallization first from petroleum ether and then from alcohol, the 2,5-dichlorodiphenyltriazene had m.p. 85-86°.

The color and form of its crystals and the coloration on dissolving in glacial acetic acid, containing α-naphthylamine, were the same as for the triazene obtained in the treatment of 2,5-dichlorodiazobenzene with phenylsulfamic acid. The melting point of a mixture of the authentic and investigated triazenes was 85-86°, indicating that they were completely identical.

b) The substance soluble in water. Above it was stated that in the condensation of 2,5-dichlorodiazobenzene with phenylsulfamic acid at pH 6, an N-sulfoazo dye was formed in 3-4% yield.

However, if the reaction was performed at pH 4, then the yield of the soluble azo dye reached 39-40%. In the latter case, the reaction precipitate had to be brought to pH 7-8 with bicarbonate before extraction with boiling water so as not to contaminate the substances isolated with products of decomposition of the triazene in an acid medium.

The hot water extract deposited a brownish-yellow powder on cooling with ice. After 2 recrystallizations from boiling water the external appearance of the powder hardly changed.

The product obtained was completely soluble in water. It did not combine with H-acid either in the cold or on heating, both in a neutral and an acid solution. On heating with an aqueous solution of mineral acid a voluminous, fine precipitate formed and the filtrate gave a precipitate of barium sulfate on adding barium chloride. On treatment with a hydrochloric acid solution of stannous chloride, the product was decolorized. The reduced solution gave a positive reaction for p-phenylenediamine with aniline hydrochloride and ferric chloride.

The reactions enumerated are characteristic of the N-sulfonate of 2,5-dichloro-4-aminoazobenzene. This supposition was confirmed by analyses for nitrogen and sulfur content.

Found %: N 11.23; S 8.55. $C_{12}H_8O_3N_3SCl_2Na$. Calculated %: N 11.41; S 8.71.

SUMMARY

1. In acidic media, diazo compounds react with phenylsulfamic acid to form diazonium phenylsulfamates, which are characterized by a strong color in the crystalline state and a weak one in an aqueous solution.

2. In media with pHs from 4 to 6, diazonium phenylsulfamates rearrange mainly into unstable diaryltriazene-N-sulfo acids, which decompose into unsymmetrical diaryltriazenes and sulfuric acid.

3. Combination at the position para to the sulfamino group with the formation of N-sulfo derivatives of 4-aminoazobenzenes is a minor part of the reaction between diazo compounds and phenylsulfamic acid.

4. An explanation for the instability of the sulfo groups in diaryltriazene-N-sulfo acids has been put forward.

5. The properties of N-sulfo derivatives of 4-aminoazobenzenes have been investigated.

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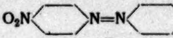
THE REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

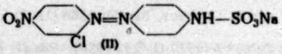
VI. THE INDICATOR PROPERTIES OF 4-AMINOAZOBENZENE-N-SULFONATES

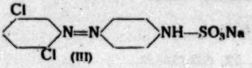
D.Z. Zavelsky and L.A. Lishnevskaya

It was shown in a previous report[*] that in reactions of diazo compounds with N-phenylsulfamic acid in solutions with pHs from 4 to 6, besides unsymmetrical diaryltriazenes, N-sulfonic acids of 4-aminoazobenzenes are formed.

The main properties of this series of dyes were described in the same report. Further investigations showed that aminoazobenzene-N-sulfonates have indicator properties both in an acidic and an alkaline medium. The following three dyes were investigated.


(I)


(II)


(III)

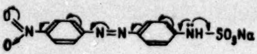
It was found that their aqueous solutions in a neutral medium were colored from yellow, for the dichloro derivative (III), to orange, for the 4-nitro-2-chloro derivative (II). On adding concentrated hydrochloric or sulfuric acids to these solutions they all acquired a strong color from red to crimson, and when diluted with water again they reverted to their original color.

At the same time the addition of caustic alkali to a neutral dye solution changed their color to cherry and purple reds, which again were converted to the original colors by neutralizing with free alkali. They gave a much weaker color with alkali carbonates which became stronger on heating.

The increase in color of N-sulfoaminoazo dyes both in an alkaline and in an acidic medium, induced us to investigate their absorption spectra in neutral, acidic and alkaline media. These curves are given in the experimental in Figures 1-3 and the characteristic indices are given in the table.

The following conclusions may be made from an examination of the absorption curves and the table given.

Dyes (I), (II) and (III) in a neutral state belong to the intramolecular-ionoidic group. In their conjugation chain, composed of two benzene nuclei, bonded by an azo group, they contain an amino group, substituted by a sulfo group, as an electron donating auxochrome, and either a nitro group (I), a nitro group and a chlorine II) or two chlorines (III) as an electron acceptor. The bond between the amino and sulfo groups without doubt hinders the participation of the free pair of electrons in conjugation with the electron acceptor auxochromes. Therefore, despite the considerable strength of the latter, the charge is apparently insufficiently displaced and as a result λ_{max} is in the 433-400 mμ range for all three dyes.



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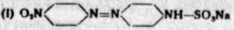
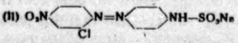
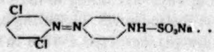
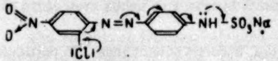
[*] See J. Gen. Chem. 27, 1330 (1957).

The Relationship λ_{max} and ϵ to the Structure of N-Sulfaminoazo Dyes and to the pH of the Medium

Dye formula	In a neutral medium		In an acidic medium		In an alkaline medium	
	λ_{max} (mμ)	$\epsilon \cdot 10^{-4}$	λ_{max} (mμ)	$\epsilon \cdot 10^{-4}$	λ_{max} (mμ)	$\epsilon \cdot 10^{-4}$
(I) 	433	1.8	510	2.3	525	3.7
(II) 	400	3.9	490	2.4	530	6.0
(III) 	410	1.9	—	—	485	4.9

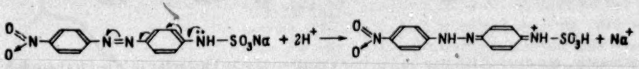
Note: Dye (III) splits off the sulfo group rapidly at room temperature in an acidic medium and is precipitated; therefore, we were unable to plot its curve in an acidic medium.

Dye (II), which differs from dye (I) only in the presence of chlorine in the position ortho to the azo group, unexpectedly has a lower value for λ_{max} (by 33 mμ) than the latter and at the same time an ϵ which is twice as great, characterizing the absorption intensity. It seems likely that the reason for such a dual effect is the double character of the chlorine atom. Having a small positive conjugation effect which opposes the direction of the conjugation due to the imino and nitro groups in dye (I), the chlorine in the ortho-position is, apparently, the reason for the hypsochromic effect, expressed by the displacement of λ_{max} towards shorter wavelengths. At the same time the considerable negative inductive effect of chlorine, added to the effect of the nitro group in the para-position which has negative conjugation and induction effects, is, apparently, the reason for doubling the molar extinction ϵ.



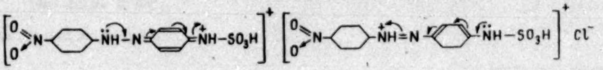
In dye (III), in which the left benzene nucleus is substituted by two chlorine atoms in the ortho- and meta-positions, λ_{max} is only 23 mμ and ϵ only slightly greater than dye (I), which contains one para-nitro group in the same nucleus.

The character of the N-sulfaminoazo dyes changes sharply in an acidic medium. In this case the proton is added not to the amino group, as might be expected, but to one of the nitrogens of the azo group due to the transfer of the reactive center along the chain of conjugated bonds [1].

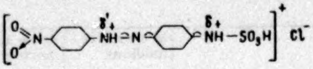


Consequently, the dyes, which are intramolecular-ionoidic ones in a neutral medium, become dye-salts in an acidic medium, in which the color is due to the complex organic cation.

It can be seen from the last equation, that as a result of the addition of the proton, the right part of the dye molecule becomes more symmetrical and due to this the positive charge, expressed in the formula on the right imino group, is actually also present on the left imino group. Therefore, the dye formula may be shown as a combination of the two extreme formulas, with curved arrows, showing the direction of electronic displacement

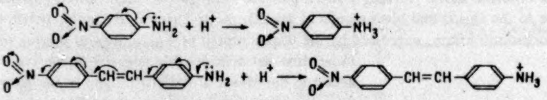


or, by B.A. Izmailsky's system [2], by one formula with fractional charges

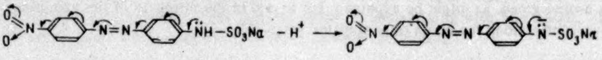


Dyes with such a structure must possess a considerably greater electron lability, than the same dyes in a neutral medium, and should, therefore, absorb light at a much longer wavelength. It can be seen from the data in the table that actually in changing from a neutral to an acidic medium λ_{max} increases by 77 for dye (I) and by 90 mμ for (II). At the same time almost complete equalization of λ_{max} and ϵ for both dyes is observed, with ϵ increasing by 30% for dye (I) and decreasing by 40% for dye (II). We consider that this phenomenon that seems inexplicable at first glance, may be explained in the following way. According to the formulas given above for N-sulfaminoazo dyes in an acidic medium, the left part of the molecule, consisting of a benzene nucleus with a nitro group in dye (I) or a nitro group and chlorine in dye (II), participate little in the conjugation whose end points are the two imino groups. It acts rather as an acidifying residue for the left imino group similarly to the sulfo group for the right imino group. As a result of this "disconnecting" of the left benzene nucleus λ_{max} and ϵ of dyes (I) and (II) are equalized, as the difference between the dyes consists only of a chlorine atom, in a "disconnected" part of the molecule.

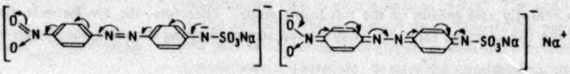
The accuracy of such a hypothesis can be confirmed by the common fact that yellow p-nitroaniline and orange-red 4-nitro-4'-aminostilbene when acidified, i.e., after the addition of a proton, become colorless or light-yellow [3], which, apparently, is due to the elimination of or strong decrease in the intramolecular conjugation between the amino and nitro groups which can be observed in a neutral medium.



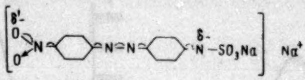
In an alkaline medium, the N-sulfaminoazo dyes being investigated, undergo new changes, in particular a proton is split off from the imino group, which is under the acidifying influence of the sulfo group directly bonded to it. The ionic charge thus freed, transmitting additional electronic density to the nitrogen of the imino group, becomes the cause of a stronger displacement of electronic density by the π-bond system of both benzene nuclei to the nitro group.



Consequently, our dyes which had an intramolecular-ionoidic character in a neutral medium and are converted into dye-cations in an acidic medium, become, after the removal of a proton, dye-anions in an alkaline medium. Here the anionic charge, which has great lability, is localized to a considerable degree due to conjugation, at the oxygen of the nitro group. The structure of, for example, dye (I) in an alkaline medium may be given as a combination of two formulas



or as one formula with fractional charges



The increase in the lability of the electronic charge in an alkaline medium, as may be expected, leads in the case of dye (I) to the displacement of λ_{max} to 525 $m\mu$, i.e., by 92 $m\mu$, and to an increase in absorption intensity ϵ by more than 2 times. In dye (II) the small positive conjugation effect of chlorine, which was the cause of the hypsochromic displacement of λ_{max} in a neutral medium, becomes unnoticeable in an alkaline medium, in comparison with dye (I), as the strong conjugation effect of the imino group anion counteracts it by acting in the reverse direction. Therefore, λ_{max} for dye (II) is displaced from 400 to 530 $m\mu$ and even becomes slightly greater than that for dye (I). At the same time, ϵ for dye (II) increases to $6.0 \cdot 10^4$, which is one and a half times as great as that for dye (I), apparently, as a result of the additional negative inductive effect of chlorine.

In dye (III), which has two chlorine atoms instead of one nitro group, an increase in λ_{max} is also observed in an alkaline medium, but by 40-45 $m\mu$ less than for dyes (I) and (II). At the same time, the absorption intensity ϵ also increases by 2.5 times and not by two times as for dye (I). Apparently, the combined inductive effects of the ortho- and meta-chlorine atoms, has a smaller effect on the increase in λ_{max}, than the effects of conjugation and induction of one para-nitro group, which at the same time have a stronger effect in increasing the molar extinction ϵ.

EXPERIMENTAL

The Na salt of 4-amino-4'-nitroazobenzene-N-sulfonic acid (I). The neutral aqueous solution of the azo dye was orange in color. On adding several drops of alkali, the solution became a cherry-red color, which disappeared on neutralization. On adding soda to a neutral solution of the dye, the solution reddened considerably less. Heating the solution, made alkaline with soda, increased the color. If concentrated hydrochloric or sulfuric acids were added to a neutral solution of the dye, the solution became crimson.

The Na salt of 4-amino-4'-nitro-2'-chloroazobenzene-N-sulfonic acid (II). The neutral aqueous solution of the dye was orange in color. On adding alkali, the solution acquired an intense violet-red color, which disappeared on neutralization. On adding soda instead of the alkali, the aqueous solution of the dye acquired a red-brown color, which intensified on heating. Concentrated hydrochloric acid gave a solution of the dye a bright pink color, which was converted to yellow on heating, due to splitting out of the sulfo group. In concentrated sulfuric acid, the N-sulfaminoazo dye dissolved with a crimson color, which changed to yellow on standing, even in the cold. In this case also the sulfo group was split out.

The Na salt of 4-amino-2',5'-dichloroazobenzene-N-sulfonic acid (III). A neutral aqueous solution of the dye was yellow in color. On adding alkali it became dark red. With soda the color was considerably weaker but intensified somewhat on heating. Concentrated hydrochloric acid or 35% sulfuric acid gave an aqueous solution of the dye a red color. However, on standing, even in the cold, acid solutions of the dyes were decolorized and in them there appeared a flocculent precipitate of a substance insoluble in water. Consequently, the sulfo group of this dye was split out in acid solution even more easily than in the first two dyes.

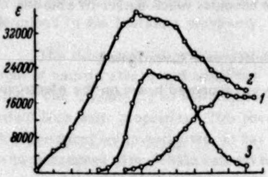
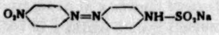


Fig. 1. Absorption spectra of  in neutral (1), alkaline (2) and acid (3) media.

Spectrophotometric investigation of solutions of N-sulfaminoazobenzenes in neutral, alkaline and acid media. A sample of the dye was dissolved in distilled water and diluted to a definite volume. To make the alkaline medium, one drop of 40% sodium hydroxide solution was added to 10 ml of the test solution. The acid medium was obtained by adding 2 ml of 70% sulfuric acid to

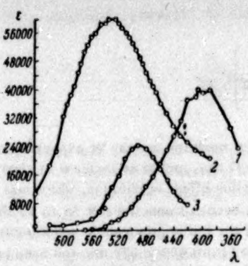
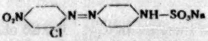


Fig. 2. Absorption spectra of



in neutral (1), alkaline (2) and acid (3) media.

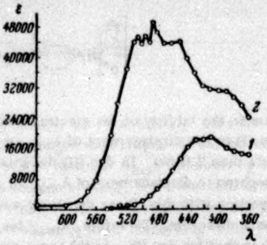
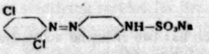


Fig. 3. Absorption spectra of



in neutral (1) and alkaline (2) media.

8 ml of the neutral solution of the dye. In the latter case the necessary correction was introduced in calculating the concentration.

The absorption spectra were plotted with an SF-4 spectrophotometer. We directly determined the optical density $D = \log \frac{I^{\circ}}{I}$ of the dye solution of known concentration at different wavelengths of the transmitted light. The value of the molecular extinction coefficient was calculated by the formula $\epsilon = \frac{1}{b \cdot c} \ln \frac{I^{\circ}}{I} = \frac{2.3}{b \cdot c} D$, where $\underline{b}$ is the thickness of the solution layer, reduced to 1 cm, and $\underline{c}$ is the concentration, reduced to 1 mole per liter.

In Figure 1 we give the absorption spectra of 4-amino-4'-nitroazobenzene-N-sulfonate in neutral (1), alkaline (2) and acid (3) media.

The wavelength λ in mμ is plotted along the abscissa and the value of the molecular extinction coefficient ε corresponding to it, along the ordinate. In Figures 2 and 3 we also give the spectra of the N-sulfonates of 4-amino-4'-nitro-2'-chloroazobenzene and 4-amino-2',5'-dichlorobenzene.

SUMMARY

1. It was shown that the color of N-sulfonates of 4-aminoazobenzenes becomes much darker in alkaline and acidic media.

2. The spectra of three dyes of the 4-aminoazobenzene-N-sulfonate series were investigated.

3. An explanation of the spectra of 4-aminoazobenzene-N-sulfonates was proposed based on the electronic theory of color of organic dyes.

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*In Russian.

SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

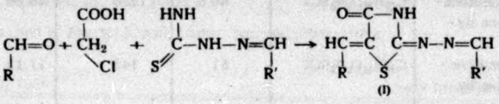
III. CONDENSATION OF MONOCHLOROACETIC ACID WITH THIOSEMICARBAZONES IN THE PRESENCE OF ALDEHYDES

E. V. Vladzimirskaya

We showed in a previous report [1], that condensation of monochloroacetic acid with p-acetaminobenzaldehyde thiosemicarbazone in the presence of an excess of aromatic aldehydes formed in one stage 5-arylidene derivatives of thiazolidinedione-2,4-p-acetaminobenzylidene hydrazone-2. In connection with this, the investigation of analogous condensations using other thiosemicarbazones seemed to be of definite interest.

For this purpose we synthesized thiosemicarbazones of benzaldehyde, anisaldehyde, o-chlorobenzaldehyde, m-nitrobenzaldehyde, cinnamaldehyde and furfurol. For the synthesis of the majority of the above thiosemicarbazones we used the method of Bernstein et al. [2].

The condensation of monochloroacetic acid with thiosemicarbazones in the presence of excess aldehyde should lead to the formation of 5,2"-diderivatives of thiazolidinedione-2,4 hydrazone-2 according to the equation



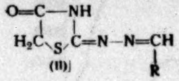
(I)

The experiments we carried out showed that this condensation actually proceeded, using o-chlorobenzaldehyde thiosemicarbazone with salicylaldehyde and anisaldehyde, m-nitrobenzaldehyde, furfurol and cinnamaldehyde thiosemicarbazones with salicylaldehyde and anisaldehyde thiosemicarbazone with o-chlorobenzaldehyde. By this method we prepared six 5,2"-diderivatives of thiazolidinedione-2,4 hydrazone-2, which have not been described in the literature previously.

The substances we synthesized have slightly acidic properties and are soluble only with difficulty in solutions of caustic alkalis and ammonia. However, one should note that they dissolve well in pyridine even in the cold. The insolubility of the preparations in 0.1 N hydrochloric acid even with boiling indicates that the preparations lack basic properties. This phenomenon eliminates the possibility of adopting thiazolenone structures for the substances we investigated, as has been accepted by some authors [3, 4] for the condensation products of thiosemicarbazones with α-halo carboxylic acids.

The preparations we synthesized, which contain salicylidene groups in their molecules, have a clearly expressed fluorescence when irradiated with ultraviolet light. Thus, the 5-salicylidene-2"-o-chlorobenzylidene derivative has a bright yellow fluorescence in the solid state, which becomes blue in an ammonia solution and light green in a sodium hydroxide solution. The 5-salicylidene-2"-m-nitrobenzylidene derivative is characterized by a bright orange fluorescence in the solid state becoming light green in an ammonia solution and yellowish-green in sodium hydroxide. 5-Salicylidene-2"-cinnamylidene and 5-salicylidene-2"-furfurylidene derivatives have a bright yellow fluorescence in the solid state, which becomes green when the preparations are dissolved in alkali or ammonia solutions.

The substances described are diarylidene derivatives of thiazolidinedione-2,4 hydrazone-2. However, as our investigations showed, the condensation of monochloroacetic acid with benzaldehyde thiosemicarbazone (in the presence of p-dimethylaminobenzaldehyde) and also with anisaldehyde thiosemicarbazone (in the presence of salicylaldehyde) resulted in the formation of a thiazolidine ring without simultaneous condensation at position 5. In the above condensations the reaction products formed a precipitate, which was difficultly soluble in boiling acetic acid. Thus, the monoarylidene derivatives (II) formed were removed from the reaction mixture and did not undergo further condensation with the aldehydes present.


(II)

The monoarylidene derivatives of thiazolidinedione-2,4 hydrazone-2 we prepared were instable substances and were hydrolyzed when heated for a short time in alkaline solutions, as shown by a positive nitroprusside reaction.

A microbiological investigation of the preparations obtained, carried out in the laboratory of the microbiology department of the Lvov Institute of Medicine (M.M. Muzyka, S.M. Kapustyak), showed that the arylidene derivatives of thiazolidinedione-2,4 hydrazone-2 had significant tuberculostatic activity.

EXPERIMENTAL

12.5 mmoles of thiosemicarbazone, 15.9 mmoles monochloroacetic acid, 12.5 mmoles of the aldehyde and 50 ml of glacial acetic acid were boiled for 1 hour under reflux. The clear solution formed usually became red on boiling. After cooling, the reaction mixture was diluted with an aqueous solution of sodium acetate and the precipitate formed was filtered off, washed with water, dried in air and recrystallized from acetic acid. The results of the investigation are given in the table.

Name of preparation	Formula	Yield (in %)	Melting point	Analysis for nitrogen (in %)	
				found	calculated
5-Salicylidenethiazolidinedione-2,4-o-chlorobenzylidene hydrazone-2	$C_{17}H_{12}O_3N_3SCl$	49.5	135°	10.86	11.24
5-Anisylidenethiazolidinedione-2,4-o-chlorobenzylidene hydrazone-2	$C_{18}H_{14}O_2N_3SCl$	51	145	11.14	11.30
5-Salicylidenethiazolidinedione-2,4-m-nitrobenzylidene hydrazone-2	$C_{17}H_{12}O_4N_4S$	82.5	about 222	14.77	15.29
5-o-Chlorobenzylidenethiazolidinedione-2,4-p-anisylidene hydrazone-2	$C_{18}H_{14}O_2N_3SCl$	68.5	260	11.55	11.30
5-Salicylidenethiazolidinedione-2,4-furfurylidene hydrazone-2	$C_{15}H_{11}O_3N_3S$	54	283 (decomp.)	13.46	13.41
5-Salicylidenethiazolidinedione-2,4-cinnamylidene hydrazone-2	$C_{19}H_{15}O_2N_3S$	43	290 (decomp.)	11.96	12.03
Thiazolidinedione-2,4-benzylidene hydrazone-2	$C_{10}H_9ON_3S$	74	259	19.18	19.17
Thiazolidinedione-2,4-p-anisylidene hydrazone-2	$C_{11}H_{11}O_2N_3S$	84	254	16.89	16.86

To confirm the structures that we put forward for the substances synthesized, we boiled 0.1-0.2 g of the 5-arylidene derivatives with 10 ml of concentrated hydrochloric acid for 3-5 hours. Thus, from the 5-salicylidene derivatives we obtained 5-salicylidenethiazolidinedione-2,4 (m.p. 230°) and from 5-o-chlorobenzylidenethiazolidinedione-2,4-p-anisylidene hydrazone-2, correspondingly, 5-o-chlorobenzylidenethiazolidinedione-2,4 (m.p.

172*). The melting points of the preparations obtained corresponded to the literature data [5, 6]. We should also mention that the melting points of the monoarylidene derivatives of thiazolidinedione-2,4 hydrazone-2 (II) corresponded to the literature data [3].

The thiazolidinedione-2,4 hydrazone-2 derivatives that we synthesized were yellow substances, except for the furfurylidene derivative, which was a light brown color. They dissolved in pyridine in the cold, in acetic acid and glycerin on heating and with difficulty in alcohol and acetone. The introduction of a substituent in position 5 increased the solubility of the preparations in chloroform and benzene. The preparations containing two arylidene groups in their molecule, dissolved with considerably more difficulty in solutions of alkalis, soda and ammonia, than the monarylidene derivatives.

SUMMARY

1. The condensation of monochloroacetic acid with thiosemicarbazones of the aromatic, aliphatic-aromatic and heterocyclic series in the presence of aromatic aldehydes leads, mainly, to the formation of 5,2"-di-derivatives of thiazolidinedione-2,4 hydrazone-2. If the 2"-monoderivative is a very difficultly soluble substance and precipitates during the reaction, it may be the only reaction product.

2. All the preparations we synthesized had acidic properties and, due to this, they should be assigned the structure of a thiazolidone-4 and not thiazolenone-4.

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SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

IV. ULTRAVIOLET ABSORPTION SPECTRA OF p-ACETAMINOBENZYLIDENE DERIVATIVES

M.M. Turkevich and E.V. Vladzimirskaya

We investigated the absorption spectra of thiazolidone-4 derivatives, especially the photosensitizing dyes, containing rhodanine residues in their molecules. Menczel [1] and A.E. Lutsky [2] investigated the spectra of rhodanine itself and its simplest derivatives and found that the absorption maxima in the region of 280-300 mμ were due to the C=O group in the thiazolidone ring. The introduction of arylidene substituents into a rhodanine molecule causes a sharp displacement of the absorption spectra towards longer wavelengths with a simultaneous increase in the absorption intensity in the longwave section of the ultraviolet.

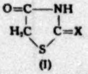
As p-acetaminobenzylidene derivatives of thiazolidone-4 have recently [3, 4] aroused definite interest as chemotherapeutic substances, we decided to study their absorption spectra in the ultraviolet and establish, where possible, the relation of the spectra to the structure of the substances investigated.

For the investigations we took thiazolidone-4 derivatives which have p-acetaminobenzylidene groupings in the 5 or 2" position. The absorption spectra of the simple basic substances, i.e., p-acetaminobenzaldehyde and its thiosemicarbazone and also thiosemicarbazide, rhodanine, pseudothiohydantoin and thiazolidinedione, were investigated for comparison.

It follows from the absorption spectra curves given in Figure 1 that the curve of p-acetaminobenzaldehyde forms a narrow band with a maximum at λ 243 mμ and a minimum at 220 mμ. A similar maximum in the region of 240 mμ was observed [6, 7] for benzaldehyde, acetophenone, benzoylacetone and is usually considered as due to the presence of a phenyl group connected to the C=O group.

The absorption curve of thiosemicarbazide resembles to a certain degree the absorption curve of p-acetaminobenzaldehyde. It is possible that this phenomenon is due to the presence of the two similar groups, C=O and C=S, in their molecules. Condensation of p-acetaminobenzaldehyde with thiosemicarbazide resulted in a considerable displacement of the spectrum intensity towards long wavelength. The long-wavelength edge of the thebone curve, was displaced by 40 mμ in comparison to p-acetaminobenzaldehyde when $\epsilon = 1000$, and by 90 mμ in comparison to thiosemicarbazide.

The maxima observed for rhodanine (I, X = S) and pseudothiohydantoin (I, X = NH), as well as the inflexion observed (Figure 2) for thiazolidinedione-2,4 (I, X = O), are due to the presence of C=O groups in the molecules of the preparations.



(I)

Thus, maxima are observed in the region of ~300 mμ for various oxo compounds of the aliphatic and aliphatic-aromatic series, as well as for acid amides [6-9]. According to the data of Wiley et al. [8], the maxima in the region of 235-255 mμ are due to a carbonyl group, whose spectrum is displaced by the effect of auxchromic groups.

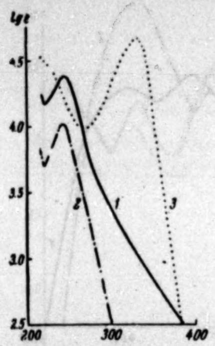
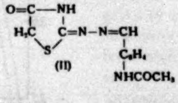


Fig. 1. Absorption spectra curves: 1) p-acetaminobenzaldehyde; 2) thiosemicarbazide; 3) thebone.

The auxchrome effect of groups connected to the C^2 atom of the thiazolidine ring, decreases in the order CS > C(NH) > CO, as the long-wavelength edge of the curves, at $\epsilon = 1000$, is at 320 mμ for rhodanine, at 275 mμ for pseudothiohydantoin and at 250 mμ for thiazolidinedione.

Figures 3 and 4 give the absorption curves of the p-acetaminobenzylidene hydrazone of thiazolidinedione-2,4 (II) and its 5-arylidene and 5-aralkylidene derivatives. The absorption intensity of the p-acetaminobenzylidene hydrazone of thiazolidinedione is considerably greater than the absorption intensity of thebone and pseudothiohydantoin.


(II)

The introduction of arylidene residues into a molecule of the p-acetaminobenzylidene hydrazone of thiazolidinedione results in a further increase in the intensity of absorption spectra in the long-wavelength region. We investigated the o-chlorobenzylidene-(III, R = o-ClC_6H_4), cinnamylidene-(III, R = $C_6H_5CH{=}CH$), p-anisylidene-(III, R = p-$CH_3OC_6H_4$) and p-acetaminobenzylidene derivatives (III, R = p-$CH_3CONHC_6H_4$), as well as the benzylidene bis-(IV, R = C_6H_5) and salicylidene bis derivatives (IV, R = o-HOC_6H_4). The long-wavelength edge of the absorption curves of the above substances, at $\epsilon = 1000$, was displaced by 60-70 mμ in comparison with substance (II).

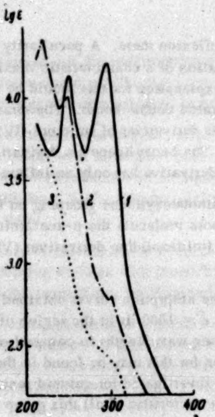


Fig. 2. Absorption spectra curves: 1) rhodanine; 2) pseudothiohydantoin; 3) thiazolidinedione.

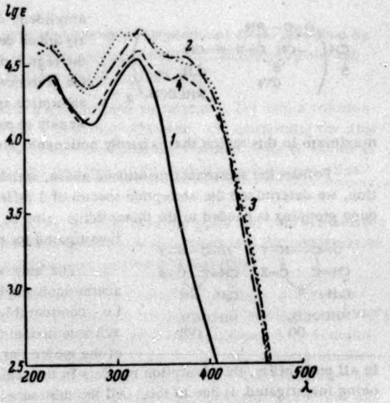
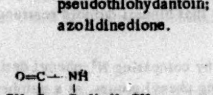


Fig. 3. Absorption spectra curves: 1) p-acetaminobenzylidene hydrazone of thiazolidinedione; 2) benzylidene bis derivative; 3) salicylidene bis derivative; 4) p-acetaminobenzylidene derivative.


(III)

The same maxima and minima were observed on the absorption curves of 5-arylidene derivatives of thiazolidinedione p-acetaminobenzylidene hydrazone as for unsubstituted p-acetaminobenzylidene hydrazone. Instead of a maximum in the region of 221-231 mμ the o-chlorobenzylidene and cinn-

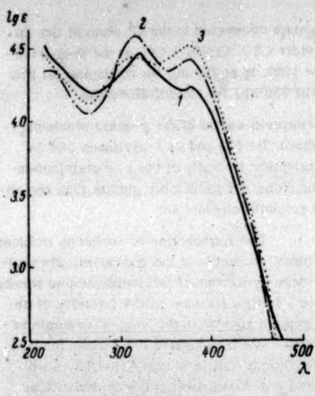


Fig. 4. Absorption spectra curves: 1) cinnamylidene derivative; 2) p-anisylidene derivative; 3) o-chlorobenzylidene derivative.

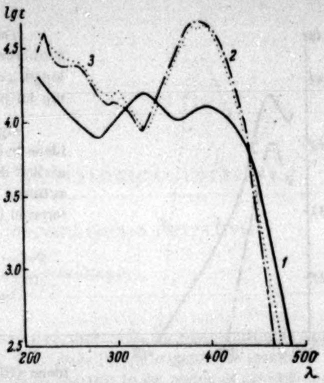
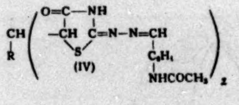
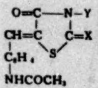


Fig. 5. Absorption spectra curves: 1) 5-p-acetaminobenzylidenethiazolidinedione-2,4; 2) 5-p-acetaminobenzylidene-3-phenyl-2-thiohydantoin; 3) 5-p-acetaminobenzylidene-2-thiohydantoin.


(IV)

amylidene derivatives form an inflexion there. A peculiarity of the 5-arylidene derivatives is the formation of a characteristic maximum in the region of 370-376 mμ. An explanation for this should be found in the presence of a chain of conjugated double bonds. The changes in the absorption spectra of arylidene bis derivatives of structure (IV) are most weakly expressed in this region. The benzylidene bis derivative has a maximum in this region that is hardly noticeable while the salicylidene derivative has only an inflexion.

Besides the substances mentioned above, which contain a p-acetaminobenzylidene grouping on the 2" position, we determined the absorption spectra of 3 different substances in whose molecule the p-acetaminobenzylidene grouping is bonded to the thiazolidine ring in position 5 (V). Two imidazolidine derivatives (VI) were also investigated for comparison.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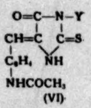
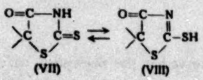

(VI)

The long-wavelength edge of the absorption curves obtained for 5-p-acetaminobenzylidene derivatives, at $\epsilon = 1000$, is in the region of ~450 mμ, i.e., considerably displaced towards long wavelengths in comparison with benzylidenerhodanine [2]. An explanation for this may be found in the capacity of the molecules of the substances we investigated for quinoid rearrangement. In all probability, the absorption maxima in the region of 394-400 mμ characteristic of all this group of substances being investigated, is due to this. All the substances containing the p-acetaminobenzylidene grouping in either positions 5 or 2", have absorption maxima in the region of 288-330 mμ, but they are less characteristic than the previous maxima. It is interesting to note that the p-acetaminobenzylidene hydrazone of 5-p-acetaminobenzylidenethiazolidinedione-2,4 (III, R = $CH_3CONHC_6H_4$) has no characteristic maximum in the region of 394-400 mμ. Apparently, the reason for this is the special spherical structure of the substance that hinders quinoid rearrangement in position 5.


(VII) (VIII)

Interesting conclusions may be drawn by comparing N^3-phenyl derivatives with analogous substances not containing phenyl groups, as a number of investigators have assumed tautomeric rearrangement occurs for rhodanine derivatives (as well as for pseudothiohydantoin, thiazolidinedione and thiohydantoin).

Ley and Specker [9] in 1939 studied the problem of the presence of lactam-lactim tautomerism for different amides by a detailed investigation of absorption spectra.

It can be seen from Figure 5 that the absorption curves of 5-p-acetaminobenzylidene-2-thiohydantoin and those of its N^3-phenyl derivative almost coincide and not only in the main maxima and minima but also in the intensity of the spectra. A similar phenomenon is observed in comparing the absorption curves of 5-p-acetaminobenzylidenerhodanine with those of its N-phenyl derivative (Figure 6). Such similarity in absorption curves proves that the substances investigated by us have a thiazolidone (VII) and not a thiazolenone structure (VIII) (or imidazolidone instead of imidazolene, respectively). This conclusion agrees with the data we obtained from chemical investigations [3, 11] which exclude a thiazolenone structure for the derivatives of rhodanine and the p-acetaminobenzylidene hydrazone of thiazolidinedione. One should also note that Lutsky's conclusion [12] on the possibility of rhodanine enolization in alkaline media, based on the noticeable displacement of the whole absorption curve with the appearance of new maxima, is questionable as rhodanine is hydrolyzed by alkali even in the cold.

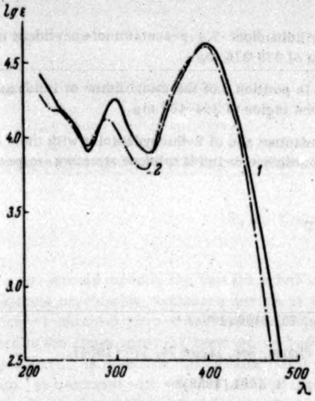


Fig. 6. Absorption spectra curves: 1) 5-p-acetaminobenzylidene -3-phenylrhodanine; 2) 5-p-acetaminobenzylidenerhodanine.

EXPERIMENTAL

We carried out the spectrophotometric investigations* with a quartz spectrophotometer SF-4, produced by the State Union Factory. The light source was a low-voltage arc hydrogen lamp VSFU-3. Solutions of the substances investigated were prepared in ethyl alcohol at concentrations of 1-2 mg/100 ml.

p-Acetaminobenzaldehyde, m.p. 153°. We prepared from p-nitrotoluene by treatment [5] with a solution of sulfur in NaOH with subsequent boiling of the reaction product with acetic anhydride. On condensing the aldehyde with thiosemicarbazide in an aqueous alcohol solution, we obtained a thiosemicarbazone (usually known as thebone) with m.p. 236°. Commercial thiosemicarbazide was used for the investigation after two recrystallizations from water.

p-Acetaminobenzylidene hydrazone of thiazolidinedione-2,4 (II), decomposition point 294°, we synthesized [3] by condensing thebone with monochloroacetic acid. On introducing aromatic aldehydes into the condensation reaction at the same time, we obtained the corresponding 5-arylidene derivatives (III) and (IV).

5-p-Acetaminobenzylidenethiazolidinedione-2,4 (V, X=O, Y=H) we prepared by heating p-acetaminobenzylidene hydrazone of thiazolidinedione (II) with hydrochloric acid and it corresponded in melting point (258°) to the preparation obtained [10] by condensing thiazolidinedione with p-acetaminobenzaldehyde. 5-p-Acetaminobenzylidenerhodanine (V, X=S, Y=H), m.p. 290°, we prepared by condensing rhodanine with p-acetaminobenzaldehyde. 5-p-Acetaminobenzylidene-3-phenylrhodanine (V, X=S, $Y=C_6H_5$), m.p. > 290°, was prepared** by the condensation of thicyanoacetic acid with phenylmustard oil in the presence of p-acetaminobenzaldehyde and lead salts. 5-p-Acetaminobenzylidene-3-phenyl-2-thiohydantoin (VI, $V=C_6H_5$), m.p. 271°, was prepared** by condensing phenylmustard oil with glycine in the presence of p-acetaminobenzaldehyde. 5-p-Acetaminobenzylidene-2-thiohydantoin (VI, Y=H), m.p. > 290° was prepared** by condensing glycine with thiocyanic acid in the presence of p-acetaminobenzaldehyde in acetic anhydride.

SUMMARY

1. The derivatives of rhodanine, pseudothiohydantoin, thiazolidinedione-2 and 2-thiohydantoin have char-

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*The measurements were performed by T.N. Gladyshevskaya.

**Preparations synthesized by V.G. Zubenko.

acteristic absorption maxima in the region of 284-330 mμ.

2. The absorption curves of 5-arylidene derivatives of thiazolidinedione-2,4-p-acetaminobenzylidene hydrazone-2 are characterized by maxima or inflexions in the region of 370-376 mμ.

3. The introduction of p-acetaminobenzylidene substituents in position 5 of the thiazolidine or imidazolidine rings results in the appearance of new absorption maxima in the region of 394-400 mμ.

4. The exceptional similarity of the absorption curves of rhodanines and of 2-thiohydantoins with those of their N^3-phenyl derivatives indicates that possibly they have a thiazolidone or imidazolidone structure, respectively.

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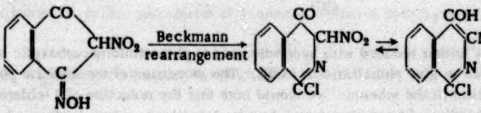
REACTION OF 1-CHLORO-3-NITRO-4-HYDROXYISOQUINOLINE WITH AMMONIA

V.N. Zelmen and G.Ya. Vanag

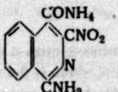
We showed recently [1], that the oxime of 2-nitroindanedione-1,3 (I) in a Beckmann rearrangement with phosphorus oxychloride, Beckmann mixture or some other chlorine-containing reagent, always gave the same substance – 1-chloro-3-nitro-4-hydroxyisoquinoline (II). The structure of this substance was, it seems, well substantiated in the above paper [1], however, we had some doubts due to the somewhat unusual behavior of the chlorine in position 1. In reduction this chlorine could not be exchanged for hydrogen but was exchanged for a hydroxyl group. In treatment with water or alkaline reagents, the chlorine, however, could not be exchanged for a hydroxyl group, i.e., we could not obtain 1,4-dihydroxy-3-nitroisoquinoline (XIV); two new substances, not containing chlorine, were obtained, one of which was formed by abstracting hydrogen chloride from 1-chloro-3-nitro-4-hydroxyisoquinoline and the other, judging by its reactions, was a hydroxamic acid. The exact structure of these substances has not yet been elucidated.



(I) (II)

We decided to investigate the reaction of 1-chloro-3-nitro-4-hydroxyisoquinoline with ammonia for a close examination of the nature of the chlorine atom. If the reaction was positive we would obtain an interesting isoquinoline derivative, containing at the same time amino and nitro groups in the pyridine ring. It is known from the literature that chlorine in position 1 in isoquinoline is labile and is readily exchanged for an amino group [2-4].

By passing dry ammonia into an alcohol solution of 1-chloro-3-nitro-4-hydroxyisoquinoline, an orangish-yellow precipitate of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline (III), was formed, which also contained ammonium chloride. The ammonium salt was soluble in water but the solution was readily hydrolyzed and we were unable to obtain the salt in a pure state. If the ammonium salt was heated with sodium hydroxide, ammonia was evolved and when cooled, a sodium salt was precipitated. This salt was pale yellow, dissolved readily in water and did not hydrolyze; therefore, it was the salt of a stronger acid. It can be seen that when treated with sodium hydroxide the ammonium salt ("phenolate") became the salt of a nitronic acid (IIIa).



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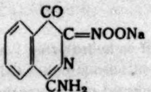

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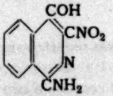

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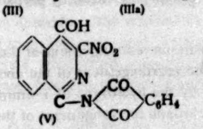

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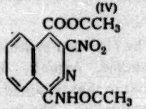
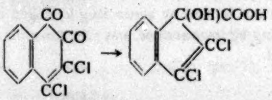


(VI)

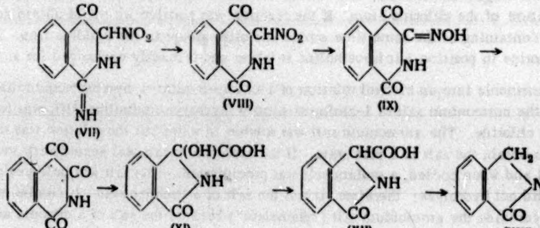
By carefully adding hydrochloric acid to the ammonium salt (III), 1-amino-3-nitro-4-hydroxyisoquinoline (IV) was precipitated, which dissolved in excess acid or in ammonia, thus indicating the double character of this compound (aminophenol or aminonitronic acid).

As proof, the amino groups of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline were condensed with phthalic anhydride in glacial acetic acid [5], and the expected 1-phthalimido-3-nitro-4-hydroxyisoquinoline (V) was obtained. It did not dissolve in water but was soluble in alkali and even in sodium bicarbonate. Acetylation of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline gave the corresponding diacetyl derivative (VI).

Reduction of 1-chloro-3-nitro-4-hydroxyisoquinoline (II) with hydriodic acid and red phosphorus gave 1,4-dihydroxyisoquinoline [1]. Reduction of 1-amino-3-nitro-4-hydroxyisoquinoline with the same reagents gave phthalimidinecarboxylic acid (XII). The mechanism of this quite unexpected reaction may, it seems, be described in the following way. 1-Amino-3-nitro-4-hydroxyisoquinoline may also exist in its tautomeric form (VII). Such a ketimine was readily hydrolyzed, of course, with the formation of compound (VIII). The nitro group of this compound was reduced to the oxime (IX) which was hydrolyzed to the triketo compound (X). Compounds of this type, as was shown in a series of papers [6-9], readily decompose hydrolytically and are rearranged. Compound (XI) was obtained as a result of this conversion, which is similar to benzylic rearrangement. A very similar conversion occurs, for example, in the structurally similar dichloro-β-naphthoquinone, which is converted into dichlorohydroxyindene carboxylic acid [10].

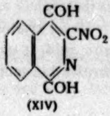


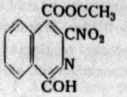
Compound (XI) was further reduced with hydriodic acid to phthalimidinecarboxylic acid (XII). The latter was readily decarboxylated to give phthalimidine (XIII). The succession of the separate phases may, of course, be different to the one given in the scheme. We should note that the reduction of 1-chloro-3-nitro-4-hydroxyisoquinoline (II) with hydriodic acid and phosphorus, besides 1,4-dihydroxyisoquinoline, also gives phthalimidinecarboxylic acid, under certain conditions.

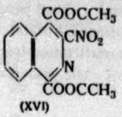


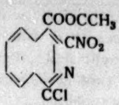
Also, the amino group was readily split off on hydrolyzing 1-amino-3-nitro-4-hydroxyisoquinoline with dilute hydrochloric acid, giving 1,4-dihydroxy-3-nitroisoquinoline (XIV), which is the tautomer of compound (VIII). The fact that compound (XIV) contained two hydroxyl groups was shown by preparing a monoacetate (probably XV) as well as a diacetate (XVI).

Compound (XIV) should also be obtained by Beckmann rearrangement of the oxime of 2-nitroindanedione-1,3 with reagents not containing chlorine. Actually, the rearrangement of the above oxime with concentrated sulfuric acid gave a product identical to that obtained by the hydrolysis of 1-amino-3-nitro-4-hydroxyisoquinoline, i.e., 1,4-dihydroxy-3-nitroisoquinoline. The Beckmann rearrangement of the oxime of nitroindanedione with sulfuric acid will be investigated separately.


(XIV)


(XV)


(XVI)


(XVII)

The acetate of 1-chloro-3-nitro-4-hydroxyisoquinoline (XVII), when treated with dry ammonia, gave the same ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline (III) as the unacetylated compound (II). When boiled with sodium hydroxide this ammonium salt was also converted into the sodium salt of the nitronic acid (IIIa).

EXPERIMENTAL

1-Amino-3-nitro-4-hydroxyisoquinoline. Dry ammonia was passed into a suspension of 10 g of 1-chloro-3-nitro-4-hydroxyisoquinoline in anhydrous alcohol. Heat was evolved and a red solution formed. On cooling it, there formed an orange-red precipitate (9.3 g) of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline (III), which also contained ammonium chloride. On dissolving in water, the salt partially hydrolyzed, forming a yellow precipitate, which again dissolved up in ammonia. On carefully adding hydrochloric acid, a precipitate formed, which dissolved in excess acid and in ammonia. On treating the dry salt with alcohol, a white residue of ammonium chloride remained. The ammonium salt separated from the alcohol solution in an amorphous form with m.p. about 188-189°.

The ammonium salt was dissolved in water with heating and filtered and hydrochloric acid was added dropwise to the red-brown filtrate. A yellow precipitate of 1-amino-3-nitro-4-hydroxyisoquinoline (IV) formed. The m.p. was 210-212°.

Found %: N 20.53. $C_9H_7O_3N_3$. Calculated %: N 20.48.

9 g of the ammonium salt was boiled with 10% sodium hydroxide. Ammonia was evolved, the solution first became an orange-red color and then yellow and fine yellow needles of the sodium salt of 1-amino-3-nitro-4-hydroxyisoquinoline precipitated. The yield was 5.5 g. It could be recrystallized from water and alcohol.

Found %: N 18.56. $C_9H_6O_3N_3Na$. Calculated %: N 18.50.

1-Phthalimido-3-nitro-4-hydroxyisoquinoline (V). 5 g of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline and 10 g of phthalic anhydride in glacial acetic acid were boiled for 1.5 hours. On cooling, the unreacted phthalic anhydride precipitated and was filtered off with suction and the filtrate was diluted with water. A yellow precipitate formed. It was boiled several times with water to free it from phthalic acid and phthalimide, formed during the reaction. After crystallization from glacial acetic acid, the residue gave fine, yellow crystals of 1-phthalimido-3-nitro-4-hydroxyisoquinoline. The m.p. was 249-250° (with decomposition). It was readily soluble in alkali, forming yellow solutions.

Found %: N 12.52, 12.54. $C_{17}H_9O_5N_3$. Calculated %: N 12.54.

1-Acetylamino-3-nitro-4-hydroxyisoquinoline acetate (VI). Acetyl chloride was poured onto 5 g of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline with cooling and stirring. When all the orange-red color had changed to light yellow, the solution was poured onto ice. The precipitate was filtered off and washed with water to remove ammonium chloride. The residual lustrous yellow crystals of 1-acetylamino-3-nitro-4-hydroxyisoquinoline acetate had m.p. 206-207° (with decomposition). On heating with zinc dust in glacial acetic acid, a red solution was first formed, which then changed to violet and finally to yellow. The latter gave only a brown coloration with a weak violet fluorescence with bindone.

Found %: N 14.57. $C_{13}H_{11}O_5N_3$. Calculated %: N 14.53.

Phthalimidinecarboxylic acid (XII). 5 g of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline, 25 ml of commercial hydriodic acid and 5 g of red phosphorus were heated until the violent reaction ceased and sucked through a glass filter. After diluting with water, the filtrate deposited a yellow, crystalline substance – phthalimidinecarboxylic acid. After crystallization from alcohol or glacial acetic acid, it was a yellow substance with m.p. 165-166° (with decomposition). The phthalimidinecarboxylic acid dissolved in sodium bicarbonate and reduced Fehling's solution.

Found %: N 8.10. $C_9H_7O_3N$. Calculated %: N 7.91.

Phthalimidine (XIII). Phthalimidinecarboxylic acid was heated on an oil bath at 170°; carbon dioxide was evolved. After recrystallization from water, the precipitate gave white crystals of phthalimidine with m.p. 149-150° (150° according to the literature).

Found %: N 10.49. C_8H_7ON. Calculated %: N 10.52.

1,4-Dihydroxy-3-nitroisoquinoline (XIV). The ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline was ground in a mortar with 2 N hydrochloric acid. The salt dissolved up. On standing, the yellow solution deposited a yellow crystalline precipitate of 1,4-dihydroxy-3-nitroisoquinoline with m.p. 229-231°. It crystallized from water, alcohol or glacial acetic acid, m.p. 233-234°. It dissolved in dilute sodium hydroxide to form an orange-red solution. On heating with zinc dust in glacial acetic acid it first formed a green solution, which then turned yellow. On standing in air, the yellow solution became blue in color. With bindone the yellow solution gave a red-violet coloration, which indicated the formation of a primary amino group in the reduction.

Found %: N 13.68. $C_9H_6O_4N_2$. Calculated %: N 13.59.

1,4-Dihydroxy-3-nitroisoquinoline acetates. Acetyl chloride was poured onto 1,4-dihydroxy-3-nitroisoquinoline and the whole was heated slightly on a water bath. The yellow substance, which did not dissolve, was changed to pale yellow material, which was separated off, washed with ether and crystallized from glacial acetic acid. The solution showed a weak blue fluorescence. The pale yellow crystals of the monoacetate melted at 206-207° (with decomposition).

Found %: N 11.37. $C_{11}H_8O_5N_2$. Calculated %: N 11.29.

The monoacetate obtained was boiled with excess acetyl chloride. After crystallization from glacial acetic acid, we obtained white crystals of the diacetate, m.p. 171-172° (with decomposition). On reducing it with zinc dust in glacial acetic acid, the solution at first became blue, then greenish and finally was decolorized. With bindone it gave only a weak red-violet coloration. The diacetate did not dissolve in water; it dissolved with decomposition in alkali, forming a yellow solution.

Found %: N 9.44, 9.68. $C_{13}H_{10}O_6N_2$. Calculated %: N 9.66.

Reaction of ammonia with 1-chloro-3-nitro-4-hydroxyisoquinoline acetate. 22 g of 1-chloro-3-nitro-4-hydroxyisoquinoline acetate in anhydrous alcohol was saturated with gaseous ammonia. We obtained 15 g of the ammonium salt of 1-amino-3-nitro-4-hydroxyisoquinoline (III). It was heated with 10% sodium hydroxide until the red solution turned yellow. It deposited, fine yellow needles of the sodium salt (IIIa), which was crystallized from alcohol.

Found %: N 18.80. $C_9H_6O_3N_3Na$. Calculated %: N 18.50.

SUMMARY

Treatment of 1-chloro-3-nitro-4-hydroxyisoquinoline with ammonia gave 1-amino-3-nitro-4-hydroxyisoquinoline. On standing with dilute hydrochloric acid it was hydrolyzed to 1,4-dihydroxyisoquinoline.

Reduction of 1-amino-3-nitro-4-hydroxyisoquinoline with hydriodic acid and red phosphorus gave phthalimidinecarboxylic acid. A hypothetical mechanism is given for this reaction.

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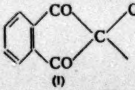
*Original Russian pagination. See C.B. translation.

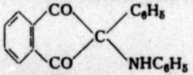
REACTION OF 2-BROMO-2-PHENYLINDANEDIONE-1,3 WITH AMINES

G.Ya. Vanag and A.K. Aren

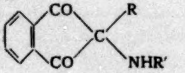
In 1893, Nathanson showed [1] that 2-chloro-2-phenylindanedione-1,3 (I) reacted with aniline forming 2-aniline-2-phenylindanedione-1,3 (II). Reactions of this type have been systematically investigated by one of us, together with Walbe [2]. Using 2-bromo-2-phenylindanedione-1,3 and 2-bromo-2-methylindanedione-1,3 as examples, it was shown that the reaction of these compounds with ammonia and amines has the same character and results in compounds of type (III). These compounds, on treatment with sodium methylate, enlarge their five-membered ring into a six-membered ring and are converted into isoquinoline derivatives (IV). A method of converting relatively common indanediones into isoquinoline derivatives was thus discovered.



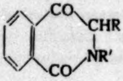
(I) X = Cl, Br



(II)



(III) $R = C_6H_5, CH_3$ $R' = H$, alkyl, aryl

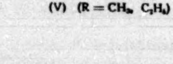


(IV)

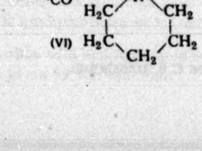
Quite recently, 2-phenylindanedione-1,3 has acquired pharmacological value: it is an effective blood anticoagulant and is finding an all increasing application in medical practice. In this connection, it was interesting to investigate the changes in the pharmacological properties of 2-phenylindanedione-1,3 on introducing an amino group into its molecule. Compounds of type (III) are aminoketones and the physiological activity of many aminoketones is generally known.

The reaction of 2-bromo-2-phenylindanedione-1,3 mainly with primary amines was investigated in the work mentioned [2]. In the present work we investigated the reaction of 2-bromo-2-phenylindanedione-1,3 with secondary and tertiary amines.

On adding dimethylamine or diethylamine to an ether solution of 2-bromo-2-phenylindanedione-1,3, dimethylamine or diethylamine hydrobromide was gradually precipitated and the corresponding tertiary base (V) remained in the solution. These were yellow, crystalline substances. Saturation of their ether solution with dry hydrogen chloride gave the corresponding hydrochlorides in the form of white, crystalline substances. The salts were soluble in water but aqueous solutions were readily hydrolyzed, the solution became yellow and a yellow base, insoluble in water, was precipitated.



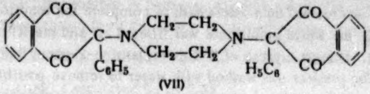
(V) ($R = CH_3, C_2H_5$)



(VI)

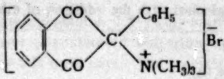
2-Phenyl-2-piperidylindanedione-1,3 (VI) was prepared similarly with piperidine. Its hydrochloride was very hydroscopic and readily hydrolyzed so that we were unable to obtain it in a pure state.

Two molecules of bromophenylindanedione reacted with piperazine forming N,N'-bis-[2-phenylindanedion-1,3-yl(2)]-piperazine (VII). Its hydrochloride was very hygroscopic. We were able to prepare the nitrate in a pure state.

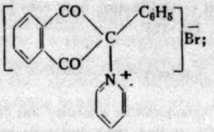


(VII)

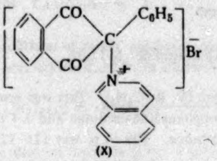
Treatment of an ether solution of 2-bromo-2-phenylindanedione-1,3 with trimethylamine gave a quaternary salt: trimethyl-[2-phenylindanedion-1,3-yl(2)]-ammonium bromide (VIII). Similarly, 2-phenylindanedion-1,3-yl(2)-pyridinium bromide (IX) was prepared from pyridine and 2-phenylindanedion-1,3-yl(2)-isoquinolinium bromide (X) from isoquinoline.



(VIII)



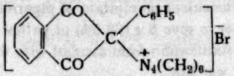
(IX)



(X)

These were white crystalline substances, readily soluble in water and alcohol and very difficultly soluble in other organic solvents. The aqueous solutions had a bitter taste and gave all the reactions characteristic of alkaloids. On standing the aqueous solutions gradually became milky white and acquired hydrophobic properties – they did not wet the walls of the tube. The white precipitate, formed after a longer period of time, did not contain nitrogen. Substances (IX) and (X) dissolved in alkalis with the red color characteristic of the enol forms of phenylindanedione. The solution was decolorized by acidification, and in the case of the isoquinolinium salt (X) a white substance was precipitated from the acid solution with m.p. about 200°, containing only half of the original nitrogen. The nature of these substances has not as yet been elucidated.

Hexamethylenetetramine gave several substances depending on the method used for the reaction. If an alcohol solution of hexamethylenetetramine was added to an alcohol solution of bromophenylindanedione, a compound was obtained which corresponded in composition to (XI). It dissolved in water with decomposition. The bromide ion was detected in the solution. It became reddish-orange in light.



(XI)

The salts prepared are being tested for physiological activity by N.S. Ratenberg in the Institute of Experimental Medicine of the Academy of Sciences of the Latvian SSR. Preliminary experiments have shown that some of these substances have spasmotherapeutic or atropine-like activity. Their negative side is their ready hydrolysis in aqueous solutions. Recently, Zaugg and Horrom [3] synthesized a series of 3-phenyl-2-amino-indanone derivatives for the purpose of testing their physiological activity. It was found that these substances were inactive physiologically. As the substances synthesized by us show a definite activity, it should be recognized that this activity is due to the indanedione group.

EXPERIMENTAL

2-Dimethylamino-2-phenylindanedione-1,3 (V, R=CH_3). Gaseous dimethylamine was passed into a solution of 15 g of 2-bromo-2-phenylindanedione-1,3 in absolute ether. The liquid became yellow or yellow-orange in color and gradually deposited a white precipitate of dimethylamine hydrobromide. When formation of the precipitate stopped, the liquid was heated on a water bath to complete the reaction and finally half the ether was distilled off. After cooling, the white precipitate was filtered off and the filtrate evaporated on a water bath or in a vacuum desiccator. Orange crystals of 2-dimethylamino-2-phenylindanedione-1,3 were deposited. The yield was 13 g (98.5%). The product was washed with water to remove possible traces of diethylamine salt and crystallized from alcohol with the addition of active charcoal. The yield was 11.1 g (84%) of a yellow, crystalline substance. The m.p. was 104-105°.

Found %: N 5.28. $C_{17}H_{15}O_2N$. Calculated %: N 5.28.

The hydrochloride. 5 g of the 2-dimethylamino-2-phenylindanedione obtained was dissolved in anhydrous ether and the solution saturated with hydrogen chloride. A fine, white, crystalline precipitate of the hydrochloride was deposited. After crystallization from anhydrous alcohol with the addition of ether, we obtained 4.2 g (74%) of a salt with m.p. 173-174°.

Found %: N 4.82. $C_{17}H_{16}O_2NCl$. Calculated %: N 4.64.

The picrate. The hydrochloride obtained was dissolved in alcohol with heating and an alcohol solution of picric acid was added. On cooling, the solution deposited yellow-green crystals of the picrate. After recrystallization from alcohol the m.p. was 201-202°.

Found %: N 11.43. $C_{23}H_{18}O_2N_4$. Calculated %: N 11.33.

2-Diethylamino-2-phenylindanedione (V, R=C_2H_5). This was prepared similarly to 2-dimethylamino-2-phenylindanedione-1,3. From 5 g of bromophenylindanedione and 3.4 ml of diethylamine in absolute ether we obtained 4 g (84%) of a yellow-orange substance. The m.p. was 116-117°.

Found %: N 4.81. $C_{19}H_{19}O_2N$. Calculated %: N 4.78.

The hydrochloride. This was prepared similarly to the hydrochloride of dimethylamino-phenylindanedione. From 5 g of diethylamino-phenylindanedione we obtained 4 g (78%) of a white, crystalline salt with m.p. 170-173°. The salt was sensitive to moisture in the air and light.

Found %: N 4.37. $C_{19}H_{20}O_2NCl$. Calculated %: N 4.25.

The picrate was prepared similarly to the previous picrate. It formed fine, yellow crystals (from alcohol). The m.p. was 188-189°.

Found %: N 10.82. $C_{25}H_{22}O_9N_4$. Calculated %: N 10.72.

2-Piperidyl-2-phenylindanedione-1,3 (VI). 5 g of 2-bromo-2-phenylindanedione-1,3 was dissolved in absolute ether and a solution of 3.5 ml of piperidine in 50 ml of anhydrous ether was gradually added to the solution with stirring. The solution rapidly became yellow colored and deposited a flocculent precipitate of piperidine hydrobromide. The filtrate was evaporated and the residue washed with water to give 5 g (98.6%) of yellow-orange 2-piperidyl-2-phenylindanedione-1,3. The m.p. was 135-137°. After recrystallization from alcohol with the addition of charcoal, the yield was 4.2 g (79.5%) of yellow crystals. The m.p. was 138°.

Found %: N 4.32. $C_{20}H_{19}O_2N$. Calculated %: N 4.58.

N,N'-Bis-[2-phenylindanedion-1,3-yl(2)]-piperazine (VII). 5 g of 2-bromo-2-phenylindanedione-1,3 was dissolved in 30-40 ml of anhydrous dioxane and a solution of 3.3 g of piperazine hydrate in 75 ml of dioxane was gradually added with stirring. The next day the precipitate was separated off and washed with dioxane and then water. A yellow crystalline substance remained on the filter. After diluting with water, the filtrate gave an identical precipitate. The total yield of N,N'-bis-[2-phenylindanedion-1,3-yl(2)]-piperazine was 4.2 g (96.6%). The substance was difficultly soluble in benzene, alcohol, ether and acetone but dissolved in pyridine and benzyl alcohol. After crystallization from the latter, it formed yellow crystals, which did not melt until 275°.

Found %: N 5.01. $C_{34}H_{26}O_4N_2$. Calculated %: N 5.32.

The dinitrate. N,N'-Bis[2-phenylindanedion-1,3-yl(2)]-piperazine was treated with concentrated nitric acid. The yellow base was converted into a colorless salt, which was washed with anhydrous benzene. On treatment with water, the salt turned yellow due to hydrolysis, forming the free base.

Found %: N 8.97. $C_{34}H_{28}O_{10}N_4$. Calculated %: N 8.59.

Trimethyl-[2-phenylindanedion-1,3-yl(2)]-ammonium bromide (VIII). 5 g of 2-bromo-2-phenylindanedione-1,3 in absolute ether was saturated with trimethylamine. A white precipitate formed. The flask was closed with a stopper and left for 2 days. The precipitate was separated and washed with ether. The yield was 3.8 g (64%) of the ammonium salt. After recrystallization from alcohol with the addition of ether, the m.p. was 123°. The salt was readily soluble in water and difficultly soluble in alcohol and other organic solvents.

Found %: N 3.44, 3.50. $C_{18}H_{18}O_2NBr$. Calculated %: N 3.89.

The picrate. A saturated aqueous solution of picric acid was added to an aqueous solution of the salt obtained. The yellow picrate precipitated was crystallized from alcohol. The m.p. was 200-201°.

Found %: N 11.14. $C_{24}H_{20}O_9N_4$. Calculated %: N 11.02.

2-Phenylindanedion-1,3-yl(2)-piperdinium bromide (IX). 3 g of piperidine in 20 ml of absolute ether was gradually added to a solution of 10 g of 2-bromo 2-phenylindanedione-1,3 in absolute ether (chloroform or carbon tetrachloride can be used) and it was heated on a water bath. A white crystalline precipitate soon appeared on the walls of the flask. The next day the contents of the flask had formed a thick, crystalline mass. It was separated and crystallized from a mixture of chloroform and alcohol. For complete isolation, ether was added. The yield of the piperidine salt was 11.3 g (89.7%), m.p. 160-162°. The salt was readily soluble in water.

Found %: N 3.43. $C_{20}H_{14}O_2NBr$. Calculated %: N 3.67.

2-Phenylindanedion-1,3-yl(2)-isoquinolinium bromide (X). This was prepared as in the previous experiment in chloroform. From 10 g of bromophenylindanedione and 4 ml of isoquinoline, we obtained 13.5 g of the white, crystalline isoquinolinium salt, m.p. 175-176°.

Found %: N 2.84. $C_{24}H_{16}O_2NBr$. Calculated %: N 3.22.

The picrate. An alcohol solution of picric acid was added to an alcohol solution of the isoquinolinium salt obtained. After crystallization from alcohol, the yellow picrate precipitated melted at 208-209°.

Found %: N 9.39. $C_{30}H_{18}O_9N_4$. Calculated %: N 9.67.

Reaction of 2-bromo-2-phenylindanedione-1,3 with hexamethylenetetramine. A solution of 0.5 g of hexamethylenetetramine in anhydrous alcohol was added to a hot solution of 1 g of 2-bromo-2-phenylindanedione-1,3 in anhydrous alcohol. The solution became greenish and deposited white, needle-like crystals on cooling, which were insoluble in alcohol. Three fractions were collected.

Found %: N 15.13 (1st fraction); 13.92 (2nd fraction); 12.55 (3rd fraction). $C_{21}H_{21}N_4Br$. Calculated %: N 12.69.

On boiling a mixture of the two components in dioxane and in alcohol other products were formed with an undetermined composition, which were often colored.

SUMMARY

The reaction of 2-bromo-2-phenylindanedione-1,3 with secondary amines gave corresponding tertiary bases. These were yellow, crystalline substances forming colorless salts with acids. These were readily hydrolyzed in aqueous solution, which shows that the tertiary bases obtained possess only weakly basic properties.

The reaction of 2-bromo-2-phenylindanedione-1,3 with tertiary amines gave the corresponding tetra substituted ammonium salts. These were colorless, crystalline substances, readily soluble in water. On standing the aqueous solutions became turbid and acquired a hydrophobic character.

Some of the compounds prepared show certain physiological activity.

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Latvian State University

COMPLEX COMPOUNDS OF MONOVALENT COPPER SALTS WITH VARIOUS ADDENDA

M.M. Azanovskaya

One can assume that complex compounds of monovalent copper with various addenda in the molecule or mixed complex compounds take part in some catalytic reactions. Nevertheless, these compounds have hardly been investigated at all.

In 1905 A.E. Arbuzov found that monovalent copper halides react with full esters of phosphorus acid, forming complex compounds of two types [1]. In compounds of the general formula $[\mathrm{CuHlog} \cdot \mathrm{P(OR)_3}]_n$ ($n = 2, 3$) (type I) there is one molecule of phosphite ester per molecule of copper monohalide. In compounds of the general formula $\mathrm{CuHlog} \cdot 2\mathrm{P(OR)_3}$ (type II) there are two molecules of phosphite ester per molecule of copper monohalide. Sometimes, compounds of the second type have been prepared by treating compounds of type I with phosphite esters.

In investigating compounds of type I, we found that they are capable of reacting with various phosphite esters and with certain other organic compounds: amines, arsines, heterocyclic, nitrogen-containing compounds and phosphines to give complex compounds of type II with various addenda in the molecule.

The reaction equation may be expressed as follows:

$$[\mathrm{CuHlg} \cdot \mathrm{P(OR)_3}]_n + n\mathrm{A} \longrightarrow n[\mathrm{CuHlg} \cdot \mathrm{P(OR)_3} \cdot \mathrm{A}]$$

$$\mathrm{Hlg} = \mathrm{Cl},\ \mathrm{Br},\ \mathrm{I};\ \mathrm{R} = \mathrm{C_2H_5},\ \mathrm{C_3H_7},\ \mathrm{C_6H_5}$$

A – phosphite ester, amine, arsine, nitrogen-containing heterocyclic compounds, etc.

The reactions were carried out by mixing the components and subsequently heating the reaction mass till a homogeneous melt formed. After cooling, the crystallized mass was recrystallized from suitable solvents. We were unable to isolate all of the compounds synthesized in the pure state due to their instability. Compounds obtained in the pure state are given in the table. The complex compounds synthesized were insoluble in water but were soluble in various organic solvents.

Expt. No.	Compound	Melting point	Molecular weight		Composition (in %)							
					P		Hlg		N		As	
			calc.	found	calc.	found	calc.	found	calc.	found	calc.	found
1	$\mathrm{CuBr \cdot P(OC_2H_5)_3 \cdot P(OC_6H_5)_3}$	66–67.5°	619.4	573	10.00	10.14	12.89	12.81	—	—	—	—
2	$\mathrm{CuI \cdot P(OC_2H_5)_3 \cdot P(OC_6H_5)_3}$	69–70.5	666.4	599	9.30	9.33	19.04	18.80	—	—	—	—
3	$\mathrm{CuBr \cdot P(OC_3H_7\text{-}iso)_3 \cdot P(OC_6H_5)_3}$	115–117	661.4	551	9.37	9.14	12.08	12.14	—	—	—	—
4	$\mathrm{CuCl \cdot P(OC_6H_5)_3 \cdot NC_5H_5}$	122–123	488	380	6.35	6.12	7.27	7.00	2.86	2.62	—	—
5	$\mathrm{CuBr \cdot P(OC_6H_5)_3) \cdot NC_5H_5}$	126–127	532.5	356	5.82	5.74	15.00	15.05	2.62	2.90	—	—
6	$\mathrm{CuBr \cdot P(OC_3H_7\text{-}iso)_3 \cdot NC_5H_5}$	108–109	430.4	451	7.20	7.51	18.09	17.82	3.25	3.02	—	—
7	$\mathrm{CuBr \cdot P(OC_6H_5)_3 \cdot NC_9H_7}$	135–136	582.4	365	5.30	5.12	13.71	13.53	2.40	2.63	—	—
8	$\mathrm{CuBr \cdot P(OC_6H_5)_3 \cdot As(C_6H_5)_3}$	116–118	759.3	551	4.08	4.02	10.52	10.86	—	—	9.89	9.63

Analysis results indicate that there are two molecules of organic material per molecule of copper monohalide in the compounds synthesized.

The molecular weight of the compounds was determined cryoscopically in a benzene solution. It was characteristic that the molecular weight found for the majority of the compounds was considerably less than the molecular weight calculated for the monomers. This indicated that the complex compounds were in a dissociated state in benzene solution. The dissociation or decomposition of the complex copper compounds in a solvent, that we discovered, is not only characteristic of this group of compounds [2]. An examination of papers in which the molecular weight of compounds of the type $[CuHlog \cdot P(OR)_3]_n$ were determined, showed that the molecular weight of most compounds of this type ($n = 3$) was tripled, but the molecular weight for compounds of the composition $CuHlog \cdot P(OCH_3)_3$, which was determined ebullioscopically in chloroform [3], was doubled and, on this basis one can assume that the triple molecule of these compounds decomposes under the conditions of the molecular weight determination.

However, due to the difference between the type of compound mentioned above and the complex compounds we synthesized, a more detailed investigation of the character of the dissociation of the latter is needed.

SUMMARY

1. It was shown that complex compounds of monovalent copper salts with phosphite esters of the type $[CuHlog \cdot P(OR)_3]_n$ react with phosphite esters, amines, arsines and heterocyclic, nitrogen-containing compounds to form complex compounds of monovalent copper salts with various addenda in a molecule of the type $[CuHlog \cdot P(OR)_3 \cdot A]$, where A is phosphite, amine, arsine or heterocyclic compound.

2. The complex compounds of monovalent copper salts we synthesized have the following compositions: $CuBr \cdot P(OC_2H_5)_3 \cdot P(OC_6H_5)_3$, $CuI \cdot P(OC_2H_5)_3 \cdot P(OC_6H_5)_3$, $CuBr \cdot P(OC_3H_7\text{-iso})_3 \cdot P(OC_6H_5)_3$, $CuCl \cdot P(OC_6H_5)_3 \cdot NC_5H_5$, $CuBr \cdot P(OC_6H_5)_3 \cdot NC_5H_5$, $CuBr \cdot P(OC_3H_7\text{-iso})_3 \cdot NC_5H_5$, $CuBr \cdot P(OC_6H_5)_3 \cdot NC_9H_7$, $CuBr \cdot P(OC_6H_5)_3 \cdot As(C_6H_5)_3$.

3. It was shown that the complex compounds synthesized were dissociated in a benzene solution.

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*In Russian.

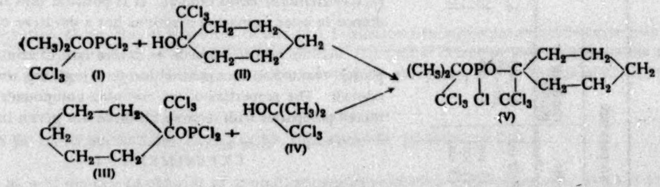
MIXED ESTERS OF TERT-(1,1,1-TRICHLORO)-BUTYL-1-TRICHLOROMETHYL-CYCLOHEXYL-1-PHOSPHORUS ACID. II.

V.S. Abramov and V.K. Khairullin

In our first report [1], we gave a short summary of the literature on attempts to prepare phosphites from tertiary alcohols and reported on our investigations of mixed esters of di-tert-(1,1,1-trichloro)-butylphosphorus acid. It was shown that acid chloridesof di-tert-(1,1,1-trichloro)-butylphosphorus acid react with primary alcohols of normal and iso structure, with secondary alcohols and with phenol in the presence of pyridine in an anhydrous ether medium, to give good yields of the corresponding mixed esters. However, the acid chloride does not react with such tertiary alcohols as acetone cyanhydrin, acetonechloroform, 1-trichloromethylcyclohexanol-1, triphenylcarbinol, and reaction with tert-butyl alcohol resulted in di-tert-(1,1,1-trichloro)-butylphosphorus acid. This behavior of the monoacid chloride and tertiary alcohols we consider to be due to steric hindrances.

The present paper describes the syntheses of esters of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid, which were prepared from the acid chloride (V) of this acid (called below the "mixed acid chloride") and various alcohols.

We prepared the mixed acid chloride by treating 1-trichlormethylcyclohexanol-1 (II) with the diacid chloride of tert-(1,1,1-trichloro)-butylphosphorus acid (I) and acetonechloroform (IV) with the diacid chloride of 1-trichloromethylcyclohexyl-1-phosphorus acid (III) in the presence of pyridine.



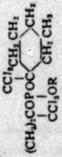
The mixed acid chloride obtained was a colorless, syrupy liquid, fuming slightly in air and distilling without decomposition. It was quite stable and after repeated distillations, unlike the mixed acid halides of the aliphatic series obtained previously [2], it underwent disproportionation.

The mixed phosphite esters were prepared from the mixed acid chloride and various alcohols. The reactions were carried out in the presence of pyridine in an anhydrous ether medium, at first with cooling and then heating to the boiling point of the ether. As a result, mixed phosphite esters were obtained with three different radicals. The primary alcohols of normal structure – methyl, ethyl, propyl, butyl – reacted very well with the mixed acid chloride to give the corresponding full mixed esters. The esters distilled well in vacuum, without decomposition. Their constants were determined. However, after a certain time the esters crystallized. When recrystallized from ether they had good melting points. The ethyl ester was obtained immediately in a crystalline state. The yields of ester were 75-85%. The esters obtained are described in Table 1 (Nos. 1-4).

Isobutyl alcohol also reacted well with the mixed acid chloride and gave a mixed ester, whose constants

TABLE 1

The Constants of Mixed Phosphite Esters



$(CH_3)_2COPOC(CCl_3)(CH_2CH_2CH_2CH_2CH_2)$ with CCl_3OR

Expt. No.	R	Temperature		d_4^{20}	n_D^{20}	MR_D		Yield (in %)	% Cl		% P	
		boiling point	melting point			found	calc.		found	calc.	found	calc.
1	CH_3	181—182.5° (2 мм)	58—60°	1.4540	1.5316	96.91	97.68	74.8	46.59	46.75	6.61	6.81
2	C_2H_5	—	86—87.5	—	—	—	—	85.1	45.21	45.37	6.48	6.60
3	n-C_3H_7	190—192 (3 мм)	44—46	1.3940	1.5235	105.93	106.92	76.5	44.07	44.04	6.18	6.41
4	n-C_4H_9	192—194 (1 мм)	—	1.3674	1.5200	110.52	111.54	76.0	43.06	42.80	6.20	6.23
5	iso-C_4H_9	189—191 (2 мм)	—	1.3742	1.5230	110.50	111.54	62.0	42.87	42.80	6.14	6.23

are given in Table 1 (No. 5).

The secondary alcohols – isopropyl and cyclohexanol – reacted with mixed acid chloride differently to the primary ones. From the reaction products of the mixed acid chloride and isopropyl alcohol, a mixed acid was isolated, identical to the product obtained by treating the mixed acid chloride with water. It was impossible to isolate any definite substances after the reaction of cyclohexanol with mixed acid chloride. The reaction products decomposed when distilled in vacuum.

Phenol did not react with the mixed acid chloride. Phenol (72%) and the acid chloride (69.5%) were recovered from the reaction products.

The reaction of the mixed acid chloride with tert-butyl alcohol gave no definite results. The wet product did not crystallize after distilling off the ether and did not react with cuprous chloride, while it decomposed on distillation in vacuum.

The formation of mixed phosphites with various alcohols is basically affected by two factors – the reactivity of the acid chloride and the alcohol and steric hindrance. The reactivity of the mixed acid chloride is less than the reactivity of the acid chloride of di-tert-(1,1,1-trichloro)-butylphosphorus acid, for example in reactions with water and alcohol, although an ether solution of the mixed acid chloride was hydrolyzed quite rapidly. The mixed acid chloride formed esters only with primary alcohols. The corresponding esters were not obtained with secondary, tertiary alcohols and phenol. This phenomenon, it seems to us, could be explained by steric hindrance. We must assume that the trichloromethylcyclohexyl grouping in the mixed acid chloride offers greater hindrance than the tert-(1,1,1-trichloro)-butyl radical. It is possible that steric hindrance in ester formation reactions has a decisive effect.

All the esters obtained, as derivatives of triatomic phosphorus, reacted with cuprous chloride [3], giving well-formed crystals. The properties of the complex compounds of the mixed phosphites with cuprous chloride are given in Table 2.

EXPERIMENTAL

Preparation of the diacid chloride of 1-trichloromethylcyclohexyl-1-phosphorus acid (III). 41.2 g of phosphorus trichloride and 65.3 g of absolute 1-trichloromethylcyclohexanol-1 in 250 ml of anhydrous ether were placed in a three-necked liter flask, fitted with a thermometer, a dropping funnel, a mechanical stirrer and a reflux condenser, closed with a calcium chloride tube. With vigorous stirring and at a temperature of 8°, 23.7 g of pyridine was added at such a rate that the temperature did not rise, after which, the mixture was stirred at room temperature for 2 hours. The pyridine hydrochloride was filtered off, the ether distilled off, and the residue distilled in vacuum. After two successive distillations, we obtained 69 g (72%) of a glycerine-like liquid, which fumed in air and on shaking, solidified into crystals of the diacid chloride of 1-trichloromethylcyclohexyl-1-phosphorus acid.

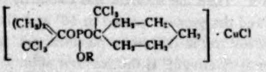
B.p. 129-130° (1 mm), m.p. 55-56°, d_4^{20} 1.5091, n_D^{20} 1.5528, MR_D 67.50; calc. 67.20.

Found %: Cl 55.42, 55.65; P 9.43, 9.47. $C_7H_{10}OCl_5P$. Calculated %: Cl 55.68; P 9.72.

Preparation of the acid chloride of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid (V). a) 158 g of the diacid chloride of tert-(1,1,1-trichloro)butylphosphorus acid (I), 126 g of 1-trichloromethylcyclohexanol-1 (II) and 53.2 g of pyridine in 500 ml of ether were placed in a flask, as described above, and the mixture boiled for 4 hours. Then the reaction mixture was cooled to room temperature. The pyridine hydrochloride was filtered off, the ether distilled off and the residue distilled in vacuum. We obtained 152 g (58.5%) of the acid chloride of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid. The b.p. was 181-182° (2 mm), d_4^{20} 1.5046, n_D^{20} 1.5422.

TABLE 2

Complex Compounds of Mixed Phosphites with Cuprous Chloride



Expt. No.	R	Recrystallization from a mixture of chloroform and methanol in ratio of	Melting point	% Cl		% P	
				found	calculated	found	calculated
1	CH_3	1:5	143-144.5°	44.67	44.80	5.48	5.59
2	C_2H_5	1:3	159-160	43.56	43.70	5.32	5.45
3	n-C_3H_7	1:4	151	42.51	42.64	5.26	5.32
4	n-C_4H_9	1:3	138-139	41.36	41.64	5.14	5.20
5	iso-C_4H_9	1:10	161-163	41.70	41.64	5.10	5.20

In a reaction of the diacid anhydride of tert-(1,1,1-trichloro)-butylphosphorus acid with a double amount of 1-trichloromethylcyclohexanol-1 and pyridine in ether, directed at obtaining the full ester of the phosphorus acid, we obtained, however, the mixed acid chloride (V) of the phosphorus acid in a yield of 61 g (75%) with similar constants.

Found %: Cl 53.82; P 6.44. $C_{11}H_{16}O_2Cl_7P$. Calculated %: Cl 54.04; P 6.74.

b) 31.85 g of the diacid chloride of 1-trichloromethylcyclohexyl-1-phosphorus acid (III) and 17.75 g of acetonechloroform (IV) in 100 ml of dioxane were placed in a half-liter three-necked flask, fitted as above. Then 7.9 g of pyridine was added dropwise at room temperature with stirring and the mixture was heated to 70-90° for 3 hours. After cooling the flask, the pyridine hydrochloride was filtered off and the dioxane distilled off at 15 mm; by distillation we obtained 14 g (30.5%) of the acid chloride (V). The b.p. was 186-188° (3 mm), d_4^{20} 1.5039, n_D^{20} 1.5421.

On hydrolysis with water, all three products gave a crystalline mixed acid with m.p. 67-69° (from cyclohexane). A mixed melting point with samples from the three experiments was not depressed.

Preparation of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid. 51.4 g of the mixed acid chloride and 2.02 g of water were placed in a 100 ml flask, which was shaken. The temperature rose from 20 to 60° with vigorous evolution of hydrogen chloride. 30 ml of ether was added and after mixing, the ether and hydrogen chloride were removed in vacuum. After a day the residue set to a compact crystalline mass of tert-(1,1,1-trichloro)-butyl-trichloromethylcyclohexyl-1-phosphorus acid with m.p. 61-64°, which was recrystallized from cyclohexane to give conglomerations of needles with m.p. 67-69°. The yield was 48 g (95%).

Found %: Cl 48.20, 47.94; P 6.69, 6.85. $C_{11}H_{17}O_3Cl_6P$. Calculated %: Cl 48.24; P 6.70.

Preparation of mixed esters of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid. 0.05 mole of alcohol and 0.05 mole of pyridine in 150-200 ml of anhydrous ether were placed in a half-liter three-necked flask, fitted with a thermometer, a dropping funnel, a mechanical stirrer and a reflux condenser, closed with a calcium chloride tube. The mixture was cooled with snow and salt and 0.05 mole of the mixed acid chloride, dissolved in 30-50 ml of ether, was added at such a rate that the temperature of the reaction mixture did not rise above +5°. After adding the acid chloride, stirring was continued at first at room temperature (1-2 hours) and then with the ether heated to boiling (30 minutes). The pyridine hydrochloride was filtered off, the ether distilled off, the pyridine hydrochloride, precipitated after distilling off the ether, filtered off again and the residue distilled in vacuum. Usually, pure ester was obtained in the first distillation. In some cases we obtained crystalline esters, which were recrystallized from ether. The constants and analyses of the esters obtained are given in Table 1.

Preparation of complexes of the mixed esters with cuprous chloride. 2-3 g of the phosphite was placed in a test tube and the calculated amount of cuprous chloride was added. The mixture was stirred with a thermometer and the rise in temperature noted. Then the mixture was carefully heated (110-120°) until the cuprous chloride almost completely dissolved and the product cooled to 40° and dissolved in chloroform. The solution was filtered and methyl alcohol was added to the filtrate in portions until a turbidity appeared. Then the mixture was heated until a clear solution was obtained; if this was not achieved, chloroform was added. On cooling, well-formed crystals were usually precipitated. The analysis and characteristics of the crystals are given in Table 2.

SUMMARY

1. We prepared the diacid chloride of 1-trichloromethylcyclohexyl-1-phosphorus acid, the mixed acid chloride of tert-(1,1,1-trichloro)-butyl-1-trichloromethylcyclohexyl-1-phosphorus acid and a mixed acid from it.

2. It was shown that with primary alcohols, the mixed acid chloride gave mixed phosphites, with three different radicals, and gave no phosphites with secondary and tertiary alcohols and phenol, which can be explained by steric hindrance.

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[2] A.I. Razumov, J. Gen. Chem. 14, 644 (1944).

[3] A.E. Arbuzov, The Structure of Phosphorus Acid and its Derivatives (St. Petersburg, 1905).**

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*Original Russian pagination. See C.B. translation.

**In Russian.

INVESTIGATION OF FURAN COMPOUNDS

IX. SYNTHESIS AND HYDROGENATION OF TERTIARY γ-FURYLALKANOLS

A.A. Ponomarev, Z.V. Til, A.D. Peshekhonova
and V.P. Reshetov

The majority of the tertiary furan alcohols, known at the present time, were prepared by Grignard synthesis, starting from pyromucic acid and its esters [1-9] or from furylalkyl or furylaryl ketones [10-12] and, therefore, contain a hydroxyl group at the carbon atom directly bonded to the furan ring. Some similar furan alcohols were converted into tetrahydrofuran ones, in yields of up to 67%, by hydrogenation over a nickel catalyst [2].

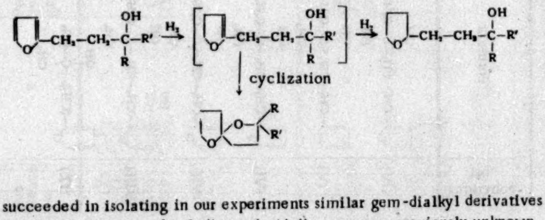
Tertiary furan alcohols, containing a hydroxyl in the side chain at a distance from the ring, were prepared by reacting CH_3MgI and C_2H_5MgBr with 1-(α-furyl)-butanone-3 [13], CH_3MgI with 1-(α-furyl)-2-methylpentanone-3 [13], as well as starting with 4-(5-methyl-2-furyl)-butanone-2 and various Grignard reagents [14].

The catalytic hydrogenation of this type of tertiary furan alcohols has not been investigated.

In the previous article [15] we reported a simple method of preparing saturated furan ketones from α,β-unsaturated ones. This makes such ketones available as starting materials for further syntheses of different types of furan substances. The present report deals with the preparation of furan alcohols using these ketones as a basis, and the catalytic hydrogenation of the former.

Under conditions of the usual Grignard synthesis, saturated furan ketones are converted into tertiary alcohols in good yields. By this method we prepared a series of tertiary alcohols with different alkyl radicals R and R' (Table 1). It is curious to note that our attempts to prepare alcohol (VII), starting with isobutylmagnesium bromide or chloride and 1-(α-furyl)-butanone-3, were completely unsuccessful, which was apparently due to the reductive activity of these Grignard reagents, already mentioned several times in the literature [16]. The alcohol mentioned was successfully obtained only by treating 1-(α-furyl)-5-methylhexanone-3 with CH_3MgI.

The hydrogenation of tertiary furan alcohols was carried out at a high temperature, under pressure, and in the presence of nickel on kieselguhr (NiK) or Raney nickel (NiR). In analogy to the corresponding primary and secondary alcohols [17, 18], in the case of tertiary γ-furylalkanols, one might have expected the formation of homologs of 1,6-dioxaspiro(4,4)nonane, besides tetrahydrofuran alcohols.



In all cases, we succeeded in isolating in our experiments similar gem-dialkyl derivatives of 1,6-dioxaspiro(4,4)nonane. This type of derivative of 1,6-dioxaspiro(4,4)nonane was previously unknown. One should note that they were formed more readily and in better yields than their isomers, prepared under the same conditions by

TABLE 1

Tertiary Furan Alcohols

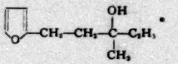
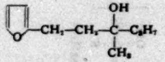
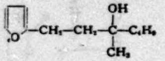
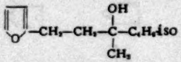
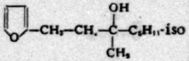
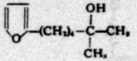
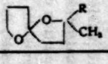
Substance No.	Formula	Starting ketone	Starting alkyl halide	Boiling point	n_D^{20}	d_4^{20}	MR_D		Found %			Calculated %			Yield (%)
							found	calc.	C	H	OH	C	H	OH	
(IV)		(I)	C_2H_5Br	81—83° (2 мм) 92—95 (5 мм)	1.4787	0.9942	47.95	48.41	—	—	—	—	—	—	87.5
(V)		(I)	C_3H_7Cl	113—114 (8 мм)	1.4756	0.9793	52.35	53.03	72.60, 72.32	10.07, 10.01	9.13	72.49	9.95	9.33	86.7
(VI)		(I)	C_4H_9Br	114—116 (3.5 мм) 120.5—121.5 (6 мм)	1.4746	0.9683	57.03	57.65	72.90	10.29	8.91	73.4	10.27	8.66	66.8
(VII)		(II)	CH_3I	115—117 (5 мм)	1.4708	0.9649	56.84	57.65	73.15	10.58	8.32	73.4	10.27	8.66	66.3
(VIII)		(I)	iso-$C_5H_{11}Br$	130—132 (7 мм)	1.4730	0.9575	61.61	62.27	74.01	10.40	8.37	74.24	10.54	8.08	80.1
(IX)		(III)	CH_3I	96— 98 (2.5 мм)	1.4731	0.9774	52.32	53.03	72.83	9.67	9.40	72.49	9.95	9.33	63.8

TABLE 2

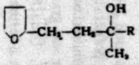
Homologs of the 1,6-Dioxaspiro(4,4)nonane Type



Substance No.	R	Prepared by hydrogenating	Boiling point	n_D^{20}	d_4^{20}	MR_D		Found (%)			Calculated (%)			Yield (in %)
						found	calc.	C	H	OH	C	H	OH	
(X)	C_2H_5	(IV) *	102—104° (45 мм)	1.4443	0.9614	47.07	47.26	70.74	10.24	None	70.54	10.66	0.0	23.7
(XI)	C_3H_7	(V)	84—86 (10 мм)	1.4466	0.9499	51.79	51.88	71.66, 71.73	11.25, 11.15	None	71.69	10.95	0.0	16.0
(XII)	C_4H_9	(VI)	99—101 (10 мм)	1.4490	0.9399	56.59	56.50	72.84, 72.89	11.38, 11.35	None	72.68	11.18	0.0	41.3
(XIII)	C_4H_9-iso	(VII)	90—93 (10 мм)	1.4470	0.9340	56.15	56.50	72.92, 73.09	11.45, 11.43	None	72.68	11.18	0.0	14.3
(XIV)	C_5H_{11}-iso	(VIII) **	107.5—109.5 (10 мм)	1.4483	0.9304	61.12	61.12	73.43, 73.05	11.68, 11.59	None	73.54	11.39	0.0	36.0

TABLE 3

Tertiary Tetrahydrofuran Alcohols of the Type



Substance No.	R	Prepared by hydrogenating	Boiling point	n_D^{20}	d_4^{20}	MR_D		Found (%)			Calculated (%)			Yield (in %)
						found	calc.	C	H	OH	C	H	OH	
(XV)	C_2H_5	(IV)	114—115° (9.5 мм)	1.4608	0.9629	49.07	49.35	69.67, 69.87	11.79, 11.76	8.82	69.72	11.70	9.87	68.9
(XVI)	C_3H_7	(V)	129—131 (10 мм)	1.4622	0.9551	53.64	53.96	70.76, 70.39	11.85, 11.73	10.37	70.95	11.90	9.67	76.0
(XVII)	C_4H_9	(VI)	115—117 (2.5 мм) 124—126 (6 мм)	1.4604	0.9407	58.35	58.58	71.89	12.21	9.11	71.95	12.08	8.49	35.0
(XVIII)	C_4H_9-iso	(VII)	130—132 (10 мм)	1.4612	0.9431	58.30	58.58	71.57	11.63	8.59	71.95	12.08	8.49	67.4
(XIX)	C_5H_{11}-iso	(VIII)	135—137 (6 мм)	1.4610	0.9327	63.06	63.20	72.79	12.46	8.28	72.85	12.23	7.94	48.0

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* On hydrogenating (IV) in the presence of NiR, (X) was obtained in 17.5% yield.

** On hydrogenating (VIII) in the presence of NiR, (XIV) was obtained in 4.5% yield.

the hydrogenation of secondary furan alcohols [18]. The physical properties (Table 2) of these compounds were found to be very close to those of their isomers with one alkyl radical, which we described previously [18].

In contrast to the starting furan alcohols, for which a depression of the molecular refraction is typical, the spirans and tetrahydrofuran alcohols were optically normal. They also had a lower density and a lower refractive index, than those typical of each group of substances, as had been found for other examples of similar compounds [17, 18].

The tertiary hydrofuran alcohols (Table 3) were thick, colorless liquids, almost without smell and stable on keeping; the spirans were more mobile, colorless liquids with a specific smell. Under certain conditions, furan and tetrahydrofuran tertiary alcohols may be readily dehydrated with the formation of furyl- and tetrahydrofurylalkenes, containing an isolated double bond in the side chain [12].

EXPERIMENTAL*

For the synthesis of tertiary furan alcohols, we used 1-(*a*-furyl)-butanone-3 (I), 1-(*a*-furyl)-5-methylhexanone-3 (II) and 1-(*a*-furyl)-hexanone-5 (III), whose preparation and properties were described previously [15]. The general method for their preparation may be summarized as follows: a solution of an equimolecular amount of the appropriate saturated ketone in absolute ether was gradually added with stirring to a solution of a Grignard reagent in absolute ether, prepared in the usual way. Usually 0.25 to 0.75 mole of the reagents was used. The magnesium alcoholate formed was decomposed with a saturated solution of ammonium chloride, the alcohol extracted with ether, the extract dried with baked sodium sulfate and after evaporating off the solvent, the product distilled in vacuum. Some physical properties of the tertiary furan alcohols, which we prepared, and analysis data are given in Table 1.

Hydrogenation of the tertiary furan alcohols was accomplished in rotating steel autoclaves (capacity 0.15 and 0.5 liters) by the usual method [17, 18] at 120° with an initial pressure of hydrogen of from 50-100 atmos. We used nickel powder on kieselguhr, freshly reduced in a current of hydrogen, equivalent to ~5% of the weight of the substance. Anhydrous ethyl alcohol was used as solvent, taking a volume not less than that of the substance.

The charge of furan alcohol was 0.25-0.75 mole. Hydrogenation was usually complete after the absorption of about 1.5 moles of hydrogen per mole of substance.

After filtering off the catalyst and distilling off the alcohol, the hydrogenate was distilled in vacuum from a Claisen flask with a pear fractionating column. At first two fractions were separated – a low-boiling one and a higher-boiling one. On redistilling each fraction in vacuum, we obtained a quite pure spiran and the corresponding tertiary tetrahydrofuran alcohol.

Data on some of the physical properties and the analyses of the homologs of 1,6-dioxaspiro(4,4) nonane, which we prepared, are given in Table 2, those of the tetrahydrofuran alcohols are in Table 3.

We should mention that the tetrahydrofuran alcohols (XV), (XVI) and (XVII) were originally prepared by one of us (Z.V. Til) by the action of C_2H_5MgBr, C_3H_7MgBr and C_4H_9MgBr on 1-(*a*-tetrahydrofuryl)-butanone-3. The determination of the percentage of hydroxyl groups was carried out in all cases by A.P. Terentyev's method [19].

SUMMARY

1. Starting with 1-(*a*-furyl)-butanone-3, 1-(*a*-furyl)-5-methylhexanone-3 and 1-(*a*-furyl)-hexanone-5 and using various Grignard reagents, the following tertiary furan alcohols were synthesized: 1-(*a*-furyl)-3-methylpentanol-3, 1-(*a*-furyl)-3-methylhexanol-3, 1-(*a*-furyl)-3-methylheptanol-3, 1-(*a*-furyl)-3,5-dimethylhexanol-3, 1-(*a*-furyl)-3,6-dimethylheptanol-3 and 1-(*a*-furyl)-5-methylhexanol-5, of which only the first was known previously.

2. It was established that hydrogenation, under pressure in the presence of nickel catalysts, of the above tertiary *γ*-furylalkanols gave, besides the corresponding tetrahydrofuran alcohols, 2,2-gem-dialkyl derivatives of 1,6-dioxaspiro(4,4)nonane. We described the properties of the five, previously unknown, tertiary tetrahydrofuran alcohols prepared by this method: 1-(*a*-tetrahydrofuryl)-3-methylpentanol-3, 1-(*a*-tetrahydrofuryl)-3-methylhexanol-3, 1-(*a*-tetrahydrofuryl)-3-methylheptanol-3, 1-(*a*-tetrahydrofuryl-3,5-dimethylhexanol-3 and 1-(*a*-

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*G. Evseeva and L.V. Popova participated in the syntheses of substances (VI), (VIII) and (XII).

tetrahydrofuryl)-3,6-dimethylheptanol-3, as well as those of the five dialkyl derivatives of 1,6-dioxaspiro(4,4)-nonane, prepared for the first time, namely: 2-methyl-2-ethyl-, 2-methyl-2-propyl-, 2-methyl-2-n-butyl-, 2-methyl-2-isobutyl- and 2-methyl-2-isoamyl-1,6-dioxaspiro(4,4)nonanes.

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*Original Russian pagination. See C.B. translation.

**In Russian.

THE SYNTHESIS OF 1-(4'-SULFOPHENYL)-3-METHYL-5-PYRAZOLONE FROM THE SODIUM SALT OF ACETOACETIC ACID

P.A. Levin

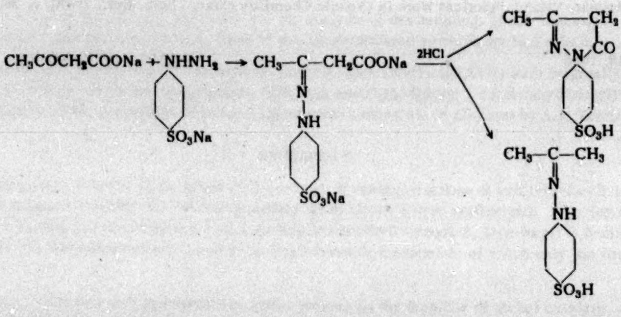
Acetoacetic ester [1, 2] is used, almost exclusively, for the synthesis of pyrazolones, such as phenylmethylpyrazolone and sulfophenylmethylpyrazolone, although in some cases the amide [3], anilide [4] and arylhydrazides [5] of acetoacetic acid may be used successfully.

Acetoacetic acid itself cannot be used for this purpose due to its instability. Its salts are more stable [6], but they, too, were not tried as starting materials for the synthesis of pyrazolones as they were considerably less accessible than most of the other derivatives of acetoacetic acid.

Nowadays, acetoacetic acid salts may be prepared readily and in quantitative yields from diketene. In connection with this, the possibility of using them as substitutes for the less available acetoacetic ester seems interesting.

The investigation of the sodium salt of acetoacetic acid as a starting material for the preparation of pyrazolones was carried out using the synthesis of 1-(4'-sulfophenyl)-3-methyl-5-pyrazolone. This pyrazolone is obtained in very low yields from acetoacetic ester [2] or by the sulfonation of phenylmethylpyrazolone [2, 7], which is also prepared from acetoacetic ester.

4-Sulfophenylhydrazine was condensed with sodium acetoacetate in an aqueous solution at normal temperature. After acidifying or heating, the process was completed by closing the pyrazolone ring. The general scheme of sulfophenylmethylpyrazolone formation, taking into account the side reaction of acetone sulfophenylhydrazone formation, is given below:



In carrying out the hydrazone formation in an alkaline medium (pH > 9), the yield of sulfophenylmethylpyrazolone was 30-40%. In a reaction medium close to neutral, the sodium acetoacetate was readily decarboxylated, especially when heated. Under these conditions, instead of the expected pyrazolone, sulfophenylhydrazine was isolated, mixed with acetone sulfophenylhydrazone.

Hydrazone formation proceeded smoothly in an alkaline medium. Approximately half of the hydrazone formed closed the ring when acidified. Besides the formation of the pyrazolone ring (acid was a catalyst for this process), decarboxylation of the unstable sulfophenylhydrazone of acetoacetic acid occurred and showed as a decrease in acidity some time after acidification. The effect of the sulfo group on the cyclization process could be seen here. It deactivated the unshared pair of nitrogen electrons and, possibly, created steric hindrance as more hydrazone should be formed with the separation of the SO_3 and COO groups from each other, i.e., that which was incapable of closing the ring underwent decarboxylation with the formation of acetone sulfophenylhydrazone. The latter is unstable in an acidic medium and may be hydrolyzed to a greater or lesser degree, depending on the reaction conditions, with the formation of the original sulfophenylhydrazine.

EXPERIMENTAL

2.5 ml (0.028 mole) of diketene was added dropwise with stirring to a 12% solution of sodium hydroxide (0.06 mole) at a temperature of 5-8°. Over a period of 10 minutes, the diketene completely dissolved in the alkali. The solution of sodium acetoacetate obtained was slowly added to a suspension of 4.85 g of 4-sulfophenylhydrazine (0.025 mole) in 45 ml of water. After 4 hours stirring, the mixture was acidified with hydrochloric acid (pH 2). After a few minutes the mixture neutralized itself (this phenomenon was not observed if for 2 hours out of the 4 the temperature was maintained at 85-95°). It was acidified 3 more times until the acid reaction remained. The following day we collected 3 g of a white crystalline precipitate; the volume of the filtrate was 90 ml.

The filtrate and the precipitate were examined without isolating the substances contained in them. By qualitative reactions (with ferric chloride, Fehling's solution, sodium nitroprusside and sodium nitrite) it was established that the precipitate contained sulfophenylmethylpyrazolone, acetone sulfophenylhydrazone and traces of sulfophenylhydrazine, which were not determined quantitatively.

The sulfophenylmethylpyrazolone was determined quantitatively by nitrosation. The sulfophenylhydrazine could be analyzed volumetrically, similarly to phenylhydrazine, using cupric hydroxide for its decomposition [8]; testing the analysis by potentiometric titration gave only an insignificant discrepancy. For analysis of the acetone sulfophenylhydrazone, we used nitrosation, which, as for sulfophenylhydrazine, gave results which were 10% high but which were reliable. The other method of analysis for hydrazone, which we used, consisted of hydrolysis by heating with hydrochloric acid (1: 5) and gasometric determination of the sulfophenylhydrazine evolved.

For analysis we prepared a solution of 0.401 g of the precipitate in 100 ml of water. After heating with hydrochloric acid, 25 ml of the solution was neutralized with 15% sodium hydroxide solution and after this 2-3 ml excess of alkali added. The alkaline solution was placed in one of the sections of the reaction vessel of a Chugaev-Tserevitinov apparatus [9] and 2-3 ml of a 15% solution of copper sulfate was placed in the other section. The liquids were mixed. The nitrogen was collected in a nitrometer. 18.8 ml of nitrogen was evolved (calculated for all the sample after correction to standard conditions).

Nitrosation was carried out on another portion of the solution. The consumption of 0.1 N sodium nitrite solution, calculated for all the sample was 17 ml.

The acetone sulfophenylhydrazone content of the precipitate was $(228 \times 18.8):22{,}400 = 0.191$ g and the consumption of $NaNO_2$ by it was $(0.191 \times 1.1):0.0228 = 9.2$ ml. The sulfophenylmethylpyrazolone content was $(17.0-9.2) \times 0.0254 = 0.198$ g. Composition of precipitate sulfophenylmethylpyrazolone 49.4%, acetone sulfophenylhydrazone 47.6%.

For analysis of the filtrate the sulfophenylhydrazine in one portion of it was first determined volumetrically. The copper base was removed by filtration. The acetone sulfophenylhydrazone in the solution obtained was determined by the gasometric method. Another portion of the filtrate was nitrosated and the consumption of $NaNO_2$ by the sulfophenylmethylpyrazolone determined, deducting the consumption by the acetone sulfophenylhydrazone and sulfophenylhydrazine from the total consumption. Composition of filtrate: sulfophenylmethylpyrazolone 0.94 g, acetone sulfophenylhydrazone 0.85 g, sulfophenylhydrazine 0.50 g.

The total yield of sulfophenylmethylpyrazolones was 38%, and of acetone sulfophenylhydrazone 39.6% (calculated on the sulfophenylhydrazine). There was 10.5% of the sulfophenylhydrazine, which did not react or was produced as a result of side reactions.

SUMMARY

1. The salts of acetoacetic acid, prepared from diketene may be used for the synthesis of pyrazolones.

2. In the condensation of 4-sulfophenylhydrazine with the sodium salt of acetoacetic acid, not less than 75-80% of the hydrazine reacts. Half of the hydrazone obtained was converted into 1-(4'-sulfophenyl)-3-methyl-5-pyrazolone. The other part, due to side reactions, was converted into acetone sulfophenylhydrazone.

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CONVERSION OF TERPENOCYCLOHEXANONES INTO FORMYLTERPENOCYCLOHEXANES, TERPENO-ε-CAPROLACTONES AND TERPENO-ε-CAPROLACTAMS

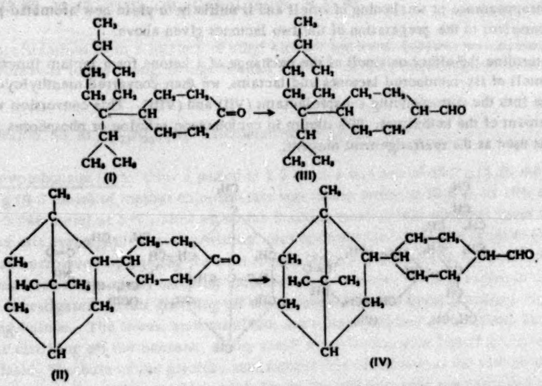
V.N. Belov and L.A. Kheifits

In order to obtain new data on the relation between the structure of organic compounds and their smell, we considered it interesting to find out how smell would be affected by a change from terpenocyclohexanones, which include aromatic principles as reported previously [1], to related compounds differing from them in the functional group.

Since of all classes of organic compounds, there is a greater number of aromatic principles among the aldehydes, we decided to trace, first of all, the change in smell in going from terpenocyclohexanones to aldehydes of similar structure, which contain one additional carbon atom in the molecule.

The simplest method of achieving such a conversion was a synthesis through the esters of the glycidic acids [2].

In the present work, we carried out the condensation of menthylcyclohexanone (I) and bornylcyclohexanone (II) with methyl chloroacetate and, without isolating the glycidic esters formed from the reaction mixture, converted them into the corresponding aldehydes (III) and (IV).

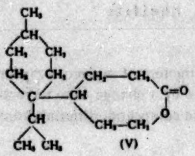


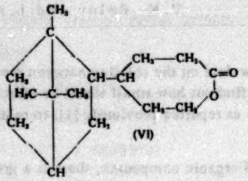
(I) (III) (II) (IV)

In contrast to menthylcyclohexanone, bornylcyclohexanone reacted with chloroacetic ester with difficulty and the greater part of the ketone was recovered from the reaction unchanged, which explained the particularly low yield of aldehyde in this case. The aldehydes obtained were rather mobile, colorless liquids and like formylcyclohexane [3], of which they are derivatives, had a strong tendency to polymerize. The smells of the compounds obtained were of no interest: menthylformylcyclohexane (III) had a lingering, fatty smell, while bornylformylcyclohexane (IV), although it had a smell somewhat reminiscent of that of menthylnonylacetaldehyde, which is a quite valuable aromatic principle, it also had a fatty smell and was considerably inferior in smell to the starting bornylcyclohexanone.

Having established that the change from terpenocyclohexanones to aldehydes of similar structure was accompanied by a deterioration in smell, and having been convinced in this way that this method showed no promise of finding new aromatic principles, we limited ourselves to applying the Darzan reaction to the above two terpenocyclohexanones.

We further undertook to find out how smell would be affected by the change from terpenocyclohexanones to the corresponding ε-caprolactones. For this purpose we used a method based on the oxidation of cyclic ketones with hydrogen peroxide or peracids. Using a mixture of hydrogen peroxide and acetic anhydride for the oxidation of menthylcyclohexanone and bornylcyclohexanone, we succeeded in preparing the corresponding ε-caprolactones (V) and (VI) in the two cases.


(V)

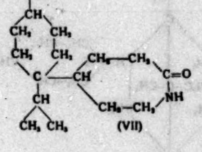

(VI)

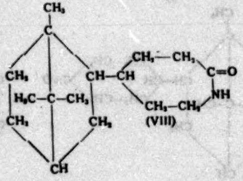
Hydrolysis of the lactones gave the corresponding ε-hydroxyacids, which were identified by preparing their silver salts.

Menthyl-ε-caprolactone (V) was a crystalline substance with no smell, and bornyl-ε-caprolactone (VI) was a viscous, slightly yellow transparent liquid with a smell reminiscent of that of the starting ketone, but weaker.

These observations, which agree with the data given earlier on the smell of other ε-caprolactones [4], apparently indicate that the conversion of substituted cyclohexanones into the corresponding ε-caprolactones is accompanied by the disappearance or weakening of smell and is unlikely to yield new aromatic principles. We therefore confined ourselves to the preparation of the two lactones given above.

In order to determine the effect on smell of the exchange of a ketone for a lactam functional group, as well as to compare the smell of six-membered lactones and lactams, we then converted menthylcyclohexanone and bornylcyclohexanone into the corresponding ε-caprolactams (VII) and (VIII). This conversion was achieved by Beckmann rearrangement of the ketoximes; 20% oleum in cyclohexane solution or phosphorus pentachloride in benzene solution was used as the rearrangement reagent.


(VII)


(VIII)

Menthyl-ε-caprolactam (VII), like menthyl-ε-caprolactone, was found to be a substance without smell, while bornyl-ε-caprolactam (VIII) had an unusual smell, somewhat reminiscent of the corresponding lactone, but even weaker. These results showed that the conversion of terpenocyclohexanones into the corresponding ε-caprolactams, the same as the conversion into the corresponding ε-caprolactones was accompanied by the disappearance or considerable weakening of the original smell.

All the compounds synthesized in this work have not been described in the literature previously.

EXPERIMENTAL

Conversion of Menthylcyclohexanone and Bornylcyclohexanone into C_{17} Aldehydes by the Darzan Reaction

Menthylformylcyclohexane (III). Over a period of 1.5 hours a mixture of 40 g (~0.17 mole) of menthylcyclohexanone and 38 g (0.35 mole) of methyl chloroacetate was slowly added with stirring to 95 g of an 18% alcohol solution of sodium ethylate (0.251 mole) at 8-10°. The contents of the flask were stirred for a further 2 hours at 5-8°, then for 2 hours at room temperature and left overnight. The next day 200 ml of a 6% aqueous sodium hydroxide solution was added to the flask and the reaction mixture stirred at 60-70° for 2 hours. On cooling the reaction mixture was extracted with ether to remove unreacted ketone and the alkaline solution acidified with 25% sulfuric acid; the acid precipitated was extracted with ether and the ether extract washed with sodium chloride solution and dried over baked sodium sulfate. After distilling off the ether, the residue was distilled in vacuum. We collected 23 g of a fraction with b.p. 146-156° (3.5 mm) containing 88% aldehyde.

After redistillation in vacuum, we isolated 15 g (35.3%) of menthylformylcyclohexane (III), containing 96.6% aldehyde.

B.p. 135-139° (2 mm), n_D^{20} 1.4901, d_4^{20} 0.9460, MR_D 76.54; calc. 76.32.

Found %: C 81.55, 81.64; H 12.12, 11.96. $C_{17}H_{30}O$. Calculated %: C 81.53; H 12.08.

Menthylformylcyclohexane is a quite mobile, colorless liquid with an unpleasant smell; it hardly distills in steam, very readily polymerizes, forming a solid substance with m.p. 185-186° (from alcohol).

Menthylformylcyclohexane semicarbazone, after 6 recrystallizations from a mixture of methyl alcohol and chloroform (4:1 by volume) formed very fine, colorless, needle-like crystals with m.p. 191-192°; it was very stable and did not decompose to yield the original aldehyde on boiling with a concentrated aqueous solution of oxalic acid and a dilute aqueous solution of sulfuric acid.

Found %: N 13.62, 13.47. $C_{18}H_{33}ON_3$. Calculated %: N 13.67.

After 4 recrystallizations from a mixture of ethyl alcohol and ethyl acetate, menthylformylcyclohexane 2,4-dinitrophenylhydrazone formed long, orange needles and melted with some signs of decomposition at 189-189.5°.

Found %: N 13.05, 13.13. $C_{23}H_{34}O_4N_4$. Calculated %: N 13.01.

Bornylformylcyclohexane (IV). Over a period of 1.5 hours a mixture of 35.2 g (0.15 mole) of bornylcyclohexanone and 32.5 g (0.3 mole) of methyl chloroacetate was slowly added to 93 g of an 18% alcohol solution of sodium ethylate (~0.246 mole) at 5-7°, after which the reaction mixture was stirred at room temperature for a further 2.5 hours and left overnight. Next day stirring was continued for a further 3 hours at 50-70° and then the reaction mixture was hydrolyzed by heating for 2 hours with 200 ml of 6% aqueous sodium hydroxide solution. After cooling, the reaction mixture was carefully extracted with benzene. This gave rise to three layers, which were separated and investigated. After distilling off the benzene from the upper, benzene, layer, we recovered 26.3 g of the starting ketone. The lower, aqueous alkali, layer was acidified with sulfuric acid and extracted with benzene; after distilling off the benzene, a very small amount (less than 1 g) of glycidic acid remained in the bottom of the flask. The bulk of the glycidic acid formed was contained, as the sodium salt, in the middle layer, which had a cherry color. After acidifying this layer, the glycidic acid was extracted with benzene, the benzene extract dried over baked sodium sulfate and after distilling off the benzene, the residue distilled in vacuum. Here, especially at the beginning, we observed a violent frothing, probably connected with the decarboxylation of the glycidic and the formation of the aldehyde, which distilled at 140-152° (3 mm). On redistillation we obtained 5 g (13.3%) of a fraction with 96.9% aldehyde content.

B.p. 140-143° (3 mm), n_D^{20} 1.4990, d_4^{20} 0.9832, MR_D 74.18; calc. 74.12.

Found % C 82.18, 82.16; H 11.26, 11.40. $C_{17}H_{28}O$. Calculated % C 82.20; H 11.36.

Bornylformylcyclohexane is a quite mobile liquid, which is extremely prone to polymerization.

After 6 recrystallizations from a mixture of methyl alcohol and chloroform (3 : 1 by volume), bornylformylcyclohexane 2,4-dinitrophenylhydrazone was obtained as red-orange needles with m.p. 175-177°.

Found % N 13.29, 13.01. $C_{23}H_{32}O_4N_4$. Calculated % N 13.08.

Oxidation of Menthylcyclohexanone and Bornylcyclohexanone to the Corresponding ε-Caprolactones

Menthyl-ε-caprolactone (V). 65 g (0.635 mole) of acetic anhydride was added slowly with stirring to 52 g of 40% hydrogen peroxide (0.635 mole); the temperature rose from 20-60°. 30 g (0.127 mole) of menthylcyclohexanone was gradually added at 50° with stirring to the oxidation mixture and also further acetic anhydride so that the reaction mixture remained clear all the time. After adding all the ketone, stirring was continued for a further 6 hours at room temperature, then for 2 hours at 50-60°, after which the reaction mixture was left overnight. Next day the oxidation mixture was distilled off from the reaction mixture (water bath and water pump) and the residue dissolved in soda solution and extracted with ether. At the boundary of the ether-water layers about 3 g of pure menthyl-ε-caprolactone collected and it was separated off, washed with water and dried; m.p. 137.5-138.5° (from alcohol), the ester number was 228 (calculated ester number 229). After distilling off the ether, we isolated about 16 g of a solid product from the ether extract, which was a mixture composed of 19% of the starting ketone (determined by oximination) and 80% lactone (determined by ester number). To separate this mixture we used the different solubilities of the ketone and the lactone in ethyl ether and also a method based on the separation of the ketone with Girard's reagent.

a) 6.5 g of the mixture of ketone and lactone was shaken twice with small portions of ethyl ether and the suspension separated off. We collected about 3.5 g of solid material, from which we obtained 2.3 g of lactone with m.p. 137-138°, after recrystallization from alcohol.

b) 5 g of Girard's P reagent was added to a solution of 8 g of the mixture of ketone and lactone in 80 ml of anhydrous alcohol and 6 g of glacial acetic acid and the mixture was boiled for 1.5 hours under reflux. After cooling, the mixture was poured into 600 g of water and ice, to which 3.9 g of pure sodium hydroxide had been added previously. The oil which separated was carefully extracted with ether and the ether extract dried over baked sodium sulfate. After distilling off the ether, we obtained about 6 g of a thick curdy mass (containing about 2% ketone), which was purified from oily impurities by drying on a porous plate. We collected about 3.5 g of a solid material, from which we obtained 1.6 g of lactone with m.p. 137-138° after two recrystallizations from alcohol.

In addition we isolated approximately 2.5 g of pure lactone from all the mother liquors. Thus, we obtained a total of 9.4 g (29%) of pure lactone.

Menthyl-ε-caprolactone is a colorless, crystalline substance without smell.

Found % C 76.24, 76.13; H 11.19, 11.19. $C_{16}H_{28}O_2$. Calculated % C 76.14; H 11.18.

After evaporation and acidification, we isolated from the soda solution about 10 g of an extremely thick oil, which was apparently a mixture of menthyl-ε-hydroxycaproic acid and its linear polyesters.

On hydrolysis, menthyl-ε-caprolactone formed menthyl-ε-hydroxycaproic acid as a finely crystalline white powder.

M.p. 104.5-105.5°. Found: acid number 208.4; % OH 12.80, 12.73. $C_{16}H_{30}O_3$. Calculated: acid number 207.5; % OH 12.58.

The silver salt of menthyl-ε-hydroxycaproic acid was a light, colorless, amorphous powder; it was insoluble in water.

Found % Ag 28.76, 28.68. $C_{16}H_{29}O_3Ag$. Calculated % Ag 28.51.

Bornyl-ε-caprolactone (VI). 34 g (0.145 mole) of bornylcyclohexanone was oxidized similarly to menthylcyclohexanone with an oxidation mixture prepared from 60 g of 40% hydrogen peroxide (0.726 mole) and 74 g (0.726 mole) of acetic anhydride. After distilling off the oxidation mixture using a water pump, the residual thick light yellow oil was mixed well with warm water and extracted with benzene. After distilling off the benzene, the residue was treated with 7% sodium bicarbonate; frothing occurred and an emulsion formed, which was destroyed by adding a small amount of alcohol. The bicarbonate solution was extracted with benzene and the benzene extract washed with sodium chloride solution and dried over baked sodium sulfate. After distilling off the benzene the residue was distilled in vacuum.

We collected a fraction with b.p. 146-165° (1 mm), containing 91% lactone (ester number 205); the ketone content of this fraction was about 7%; the yield was 13 g. On redistilling we collected a narrower fraction with a 98.4% lactone content (ester number 220.5, calculated ester number 223.9); this fraction did not contain ketone.

The yield of bornyl-ε-caprolactone, which is a very viscous, clear liquid, was 6.2 g (16.3%).

B.p. 167-172° (1.5 mm), n_D^{20} 1.5020, d_4^{20} 1.0352, MR_D 71.37; calc. 71.14.

Found %: C 76.87, 76.89; H 10.51, 10.52. $C_{16}H_{26}O_2$. Calculated %: C 76.75; H 10.47.

After evaporation and acidification, we isolated from the bicarbonate solution about 7 g of a very viscous oil, which apparently, as in the previous case, was a mixture of bornyl-ε-hydroxycaproic acid and its linear polyesters.

On hydrolysis, bornyl-ε-caprolactone formed bornyl-ε-hydroxycaproic acid as a very viscous, yellowish oil, which solidified but did not crystallize on cooling; the acid number was 206.3 (calculated acid number 208.6). After standing for 3 days, the acid number decreased to 125 and the ester number increased from 0 to 105, apparently due to self-lactonization of the acid.

The silver salt of bornyl-ε-hydroxycaproic acid was a slightly greyish amorphous powder, which was insoluble in water.

Found %: Ag 28.80, 28.92. $C_{16}H_{27}O_3Ag$. Calculated %: Ag 28.75.

Conversion of Menthylcyclohexanone and Bornylcyclohexanone into the Corresponding ε-Caprolactams

Menthylcyclohexanone oxime. A solution of 8.8 g (0.127 mole) of hydroxylamine hydrochloride in 60% ethyl alcohol was added to an alcohol solution of 20 g (0.0846 mole) of menthylcyclohexanone and after half an hour the hydrochloric acid formed was titrated with an aqueous solution of sodium hydroxide in the presence of bromophenol blue. The precipitated oxime was filtered off, ground in a mortar with a small amount of alcohol and sucked off on a glass filter. The oxime melted at 127-128°; the yield was almost quantitative.

Menthyl-ε-caprolactam (VII). 15 g of oxime was dissolved with gentle heating in 200 ml of cyclohexane and after cooling to room temperature, 20 g of oleum (20%) was added to the solution with stirring; the temperature immediately rose to 45°. After half an hour the mixture was heated till the cyclohexane boiled, while stirring, and was stirred at this temperature for 2 hours. After cooling the cyclohexane layer was washed with soda and sodium chloride solutions and dried over baked sodium sulfate. After distilling off the cyclohexane no residue at all was left in the bottom of the flask; this indicated that all the reaction product was contained in the sulfuric acid layer. The sulfuric acid layer was neutralized with 20% potassium hydroxide solution with stirring and efficient cooling and extracted several times with chloroform. After distilling off the chloroform, there remained in the flask a substance, which quickly crystallized and which, after two recrystallizations from alcohol, yielded pure menthyl-ε-caprolactam as lustrous, heavy rhombic crystals with m.p. 157.5-158.5°; a mixture with the starting oxime melted at 120°. The yield was 7g (43.8%).

Found %: N 5.59, 5.70. $C_{16}H_{29}ON$. Calculated %: N 5.57.

Bornylcyclohexanone oxime. This was prepared similarly to menthylcyclohexanone oxime, but with the difference that it was purified by distillation in vacuum. We obtained 32.5 g (87%). The very viscous oil quickly vitrified at room temperature and liquified again on heating.

B.p. 175-177° (1.5 mm), n_D^{20} 1.5192, d_4^{20} 1.0275, MR_D 73.69; calc. 73.69.

Found %: N 5.73, 5.93. $C_{16}H_{27}ON$. Calculated %: N 5.62.

Bornyl-ε-caprolactam. a) 10 g of oleum (20%) was added with stirring to a solution of 9 g (0.036 mole) of bornylcyclohexanone oxime in 150 ml of cyclohexane; the temperature immediately rose to 47°. Stirring was continued for a further 2 hours, after which the sulfuric acid layer was separated, neutralized with 20% potassium hydroxide solution with stirring and efficient cooling, extracted several times with chloroform and after distilling off the chloroform, the residue distilled in vacuum. We collected a fraction with b.p. 175-187° (2 mm); the yield was 6 g (61.6%).

b) 15 g of powdered phosphorus pentachloride was added with stirring to a solution of 10 g (0.043 mole) of oxime in anhydrous benzene. A momentary heating up was observed (the benzene boiled up), after which the temperature slowly fell to that of the room. Stirring was continued for 1.5 hours, then the reaction mixture was poured into water and ice, the benzene layer separated, washed with sodium bicarbonate solution and then water and dried over baked sodium sulfate. After distilling off the benzene, the residue, which in this case was considerably lighter than in the first case, was distilled in vacuum. We collected a fraction with b.p. 178-184° (1.5 mm); the yield was 7 g (65.4%). Distillation in vacuum at a pressure of 1-2 mm was accompanied in both cases by slight decomposition and the reaction product had a slight smell of ammonia after distillation.

To obtain a purer sample of the lactam, the reaction product from the two experiments was combined and distilled in high vacuum. No signs of decomposition were observed.

B.p. 130-132° (10^{-2} mm), n_D^{20} 1.5183, d_4^{20} 1.0344, MR_D 73.09; calc. 73.10.

Found %: C 77.18, 77.08; H 10.90, 10.98; N 5.52, 5.41. $C_{16}H_{27}ON$. Calculated %: C 77.05; H 10.91; N 5.62.

Bornyl-ε-caprolactam is a clear yellow substance, which vitrifies at room temperature.

SUMMARY

1. In order to determine how smell would be affected by the exchange of a ketone functional group for aldehyde, lactone and lactam groups, we converted menthylcyclohexanone and bornylcyclohexanone into menthylformylcyclohexane and bornylformylcyclohexane, respectively, and also into the corresponding ε-caprolactones (menthyl-ε-caprolactone and bornyl-ε-caprolactone) and ε-caprolactams (menthyl-ε-caprolactam and bornyl-ε-caprolactam).

2. It was shown that the change from menthylcyclohexanone and bornylcyclohexanone to the corresponding ε-caprolactones, ε-caprolactams and aldehydes, containing one additional carbon atom, lead to a deterioration and weakening or complete disappearance of the smell.

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**In Russian.

A NEW SYNTHESIS OF IRONE

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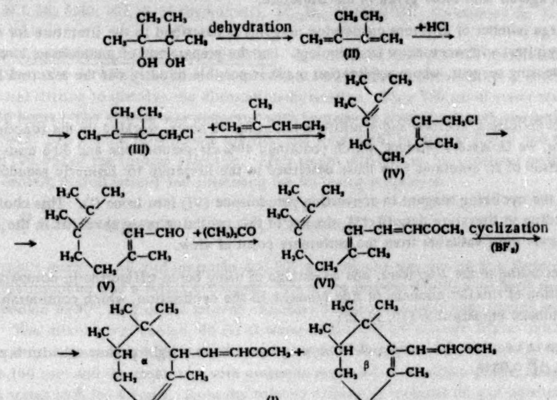
Irone, which has the delicate smell of violets, is one of the most valuable aromatic principles known at present. After the structure of irone was established as 6-methylionone, it was possible to use the rich experience accumulated in developing methods of preparing ionone preparations in the synthesis of this valuable aromatic principle. The main difficulty, however, is the preparation of 3-methylcitral or its related compounds required for the synthesis of irone. The difference in most of the systems proposed lies precisely in the different approach to the preparation of these intermediates. In some investigations attempts were made to synthesize the required carbon skeleton without the intermediate stage of preparing methylcitral or compounds similar to it, but these methods were found to be no simpler.

We carried out a new synthesis of irone (I), based on the use of isoprene and pinacone as the main starting products. The general scheme of the synthesis may be expressed as follows:



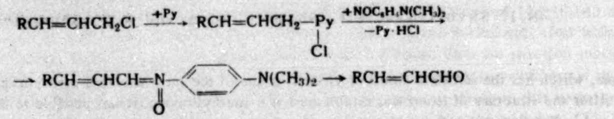
We prepared dimethylbutadiene (II) by several methods described in the literature [1-3]. Hydrochlorination of dimethylbutadiene was carried out in the usual way by saturating the diene with a calculated amount of dry gaseous hydrogen chloride.

As was recently shown [4], the addition of hydrogen chloride to dimethylbutadiene resulted in the formation of a mixture of 1-chloro-2,3-dimethylbutene-2 (III) (addition at the 1,4-position) and 3-chloro-2,3-dimethylbutene-1 (addition at the 1,2-position) besides the product of the addition of two HCl molecules. We used a wide fraction of isomeric hydrochlorides* for further reaction with isoprene.

We reacted the dimethylbutadiene hydrochlorides with isoprene – the preparation of methylgeranyl chloride (IV) – by the method recently developed by K.V. Leets [5], i.e., in a methylene chloride medium using stannic chloride as catalyst. Methylgeranyl chloride was converted into methylcitral (V) by various methods – by Krenke's method and by Sommle's method.

The Krenke reaction, which has hardly been investigated at all, is a rarely-used method of converting chlorides into the corresponding aldehydes and only a few individual cases of the preparation of α-ketoaldehydes and α,β-unsaturated aldehydes, among them citral [6], have been described in the literature.

The conversion of an α,β-unsaturated chloride into an aldehyde by Krenke's reaction may be expressed in a general form by the following scheme:



Several yields of aldehydes, prepared by Krenke's method, are mentioned in the literature. Thus, for example, the citral yield was approximately 20%.

All our attempts to increase the yield of methylcitral by improving the reaction conditions with geranyl chloride and also with methylgeranyl chloride did not give positive results.

In carrying out Sommle's reaction, we used the recently proposed improvements to prepare the reaction product of geranyl chloride and urotropin [7] and to decompose the complex formed [8]. The constants of the methylcitral obtained agreed with those given in the literature.

The use of a large number of different condensing reagents is described in the literature for the condensation of citral or methylcitral with acetone or its homologs. For the preparation of pseudoirone, we used sodium sulfite – a mild, condensing reagent, whose application made it possible to carry out the reaction at room temperature.

After mixing methylcitral, acetone and a sulfite solution for 72 hours, working up the reaction product and distilling it in vacuum, we isolated a product, which contained 40% cis-pseudoirone and 60% trans-pseudoirone, as shown by a comparison of its constants with those described in the literature for isomeric pseudoirones.

We used BF_3 as the cyclizing reagent in converting pseudoirone (VI) into irone (I). This choice was based on the fact that according to literature data [9-11], the use of this cyclizing reagent results in the formation of the stereoisomers of irone most valuable from the perfumery point of view.

Furthermore, according to the literature, one advantage of using boron trifluoride in comparison with other reagents, is the formation of smaller amounts of side products in the cyclization, which considerably lower the perfumery quality of ionone preparations [10, 12, 13].

After distillation in vacuum, the sample of irone we prepared was a light yellow oil with b.p. 95-96° (0.75-0.80 mm), n_D^{18} 1.5050, d_4^{18} 0.9343.

EXPERIMENTAL

1. Hydrochloride of 2,3-dimethylbutadiene (II). We prepared the dimethylbutadiene used by dehydration of pinacone; b.p. 69-70°, n_D^{20} 1.438.

Literature data: b.p. 69-70°; n_D^{20} 1.438 [14]; after distillation on a column with an efficiency of 25 theoretical plates b.p. 68.6° (762 mm), n_D^{20} 1.439 [2].

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*For simplicity, only one of the hydrochlorides of dimethylbutadiene, namely, the 1,4-addition compound, is given in the above scheme.

The hydrochlorination of dimethylbutadiene was carried out in an ice-cooled vessel fitted with a reflux condenser and a porous plate submerged in the layer of diene, connected to a tube for introducing the hydrogen chloride. Saturation was discontinued when the calculated gain in weight had been achieved. The unreacted dimethylbutadiene was distilled off and the reaction product distilled, when a fraction of hydrochlorides was collected with b.p. 35-60° (50 mm). The yield was 90%.

Literature data for the isomeric hydrochlorides [4]: 1-chloro-2,3-dimethylbutene-2 b.p. 57° (45 mm); 3-chloro-2,3-dimethylbutene-1 b.p. 32° (45 mm).

2. Treatment of 2,3-dimethylbutadiene hydrochlorides with isoprene. A mixture of 250 g of 2,3-dimethylbutadiene hydrochlorides, 144 g of isoprene and 585 g of methylene chloride was placed in a flask fitted with a stirrer, a dropping funnel, a thermometer and a reflux condenser. The mixture was cooled to 15° and 30 ml of a 1% solution of stannic chloride in methylene chloride was added from the dropping funnel. After 20 minutes 200 ml of a saturated solution of sodium chloride was added. The upper layer was separated, washed with saturated sodium chloride solution and the methylene chloride and excess isoprene distilled off; the residue – methylgeranyl chloride – was distilled in vacuum to yield a fraction 76-78° (2 mm). The yield was 62 g (15.8%, calculated on the hydrochlorides taken or 30.5%, calculated on the hydrochlorides reacted).

n_D^{20} 1.4818, d_4^{20} 0.9305, MR_D 57.18. $C_{11}H_{19}ClF_2$. Calculated 56.93.

Bromine number 166.6; % Cl 18.20 (hydrolysis). $C_{11}H_{19}Cl$. Calculated bromine number 171.2; % Cl 19.00.

3. Preparation of methylcitral. a) By Krenke's method (formation of pyridinium salt). A mixture of 50 g of freshly redistilled methylgeranyl chloride and 16.3 g of anhydrous pyridine was heated for 5 hours at 60-65°. On cooling, the upper oily layer was poured off and the lower dissolved in water (1:5) and extracted several times with ether, after evaporation under reduced pressure. We obtained 37 g (71%) of a light red oil, corresponding to the salt of a tertiary base.

Found %: N 5.58, 5.40; Cl 13.60 (hydrolysis). $[C_{11}H_{19}\cdot C_5H_5N]^+Cl^-$. Calculated %: N 5.27; Cl 13.30.

Conversion of pyridinium salt into methylcitral. A mixture of 36.7 g of the pyridinium salt, 20.7 g of nitrosodimethylaniline, 370 ml of alcohol and 9.5 ml of 1 N NaOH solution was kept for 3 hours at room temperature with occasional stirring to dissolve the nitrosodimethylaniline. Then 780 ml of water was added and it was kept on ice for 20 hours. The nitrone was extracted with benzene (2.5 kg of solvent), decomposed with 2 N HCl solution, washed with 10% sodium bicarbonate solution and water until neutral to litmus and the solvent distilled off to yield 7.2 g (20.6%) of the impure aldehyde. After steam distillation, we obtained methylcitral with an 86.6% aldehyde content (oximination) and possessing the following properties:

n_D^{20} 1.4915, d_4^{20} 0.9141, MR_D 52.72. $C_{11}H_{18}OF_2$. Calculated 52.07.

b) By Sommle's method. 50 g of urotropin and 200 g of toluene was placed in a three-necked flask, fitted with a stirrer, a thermometer and a reflux condenser, part of the toluene distilled off until the temperature of the vapor was 110°, cooled to 90°, 58 g of the terpene chlorides added and heated with stirring on a boiling water bath for 3 hours. The mixture was cooled, 60 ml of water added and the mixture stirred until the precipitate dissolved. The toluene solution containing the unreacted chlorides was separated off, part of the toluene distilled off in vacuum at 150 mm and the treatment with urotropin repeated as described above, using 10 g of urotropin and heating on a water bath for 4 hours. From the toluene extract we isolated 30 g of unreacted terpene chlorides.

The aqueous solutions of complex obtained were combined, 100 ml of formalin added and the solution saturated with sodium chloride. Steam was passed through a steam distillation flask and the solution of complex gradually added from a dropping funnel at such a rate that the methylcitral formed distilled off with the steam. The cooled distillate was extracted with toluene, the toluene distilled off and the methylcitral distilled in vacuum. The yield of distilled methylcitral was 10 g (19.4%, calculated on the chlorides used, or 40%, allowing for those recovered).

B.p. 92-93° (5 mm), n_D^{20} 1.4910; aldehyde content (oximination, calculated for methylcitral) 99.5%.

Literature data: b.p. 116-117° (10 mm), n_D^{20} 1.4935; aldehyde content 75% [15]. B.p. 93-94° (2.5 mm), n_D^{20} 1.4885, aldehyde content 90.3% [16]. B.p. 56-58° (0.014 mm), n_D^{20} 1.4899, aldehyde content 99.8% [17].

4. Condensation of 3-methylcitral with acetone. A mixture of 7.3 g of methylcitral, 12.0 g of acetone and 14.5 g of 11% sodium sulfite solution was stirred for 72 hours at 18-25°, the aqueous layer separated and treated 3 times with ether. The ether extracts were combined with the main product and washed successively with dilute acetic acid and sodium chloride solutions until neutral to litmus. After drying and distilling off the solvent, the crude pseudoirone (7.0 g) was distilled in vacuum, when4.3 g was collected.

B.p. 124-126° (0.6 mm), n_D^{18} 1.5348, d_4^{18} 0.9045, MR_D 70.98. $C_{14}H_{22}OF_3$. Calculated 65.46.

Literature data: b.p. 105-110° (0.12 mm), d_4^{18} 0.9048, n_D^{18} 1.5310 [18]. Cis-pseudoirone – n_D^{20} 1.5305; trans-pseudoirone – n_D^{20} 1.53732, d_4^{20} 0.9665. A mixture of cis- and trans-pseudoirone, containing 67.4% of the trans-isomer – n_D^{20} 1.53508 [9]. B.p. 94-96° (0.1-0.15 mm), n_D^{20} 1.5329 [10]; b.p. 127-128° (3.2 mm), n_D^{20} 1.5345 [15].

5. Cyclization of pseudoirone. 3.9 g of pseudoirone and 70 ml of anhydrous benzene was placed in a flask, fitted with a stirrer, a thermometer, a reflux condenser and a tube for passing in boron trifluoride. After cooling the mixture to 0-2°, it was stirred vigorously and saturated with boron trifluoride,* which was first purified and dried, using a series of columns with appropriate fillings. During the process the temperature of the reaction mixture gradually rose and 40-50 minutes after the start of saturation it reached 10°. Saturation was stopped when the boron trifluoride was no longer absorbed by the liquid. The increase in weight was about 2 g. The saturation product, which was dark brown in color, was again cooled to 0-2° and 95 ml of 8% sodium hydroxide solution was added to it slowly with stirring, and this considerably lightened the color of the benzene solution. The layers were separated and the lower layer extracted twice with benzene.

The combined benzene layers were washed with saturated sodium chloride solution until neutral to litmus. After distilling off the solvent, the residue was again treated with 25% sodium hydroxide solution for 1 hour at 30°. The lower layer was separated and extracted twice with ether and the ether extracts combined with the bulk of the material. After washing till neutral to litmus, drying and distilling off the solvent, the crude product (3.8 g) was distilled in vacuum, when the following fractions were collected: 1st 94-95° (0.9 mm), 0.8 g, n_D^{18} 1.5039; 2nd 95-96° (0.75-0.8 mm), 1.7 g, n_D^{18} 1.5050; d_4^{18} 0.9343; 3rd 96-97° (0.75-0.8 mm), 0.5 g, n_D^{18} 1.5062; residue 0.5 g.

Literature data for samples of irone, also prepared in the presence of BF_3 and fractionally distilled: b.p. 87-87° (0.15 mm), n_D^{20} 1.5042, d_4^{20} 0.9308, MR_D 65.65, $\sum MR_D$ + 1.92 [20]; b.p. 85-88° (0.05 mm), n_D^{18} 1.5021, d_4^{18} 0.9453, MR_D 65.10, $\sum MR_D$ + 1.37 [18]; n_D^{20} 1.50215, d_4^{20} 0.9344 [10]; n_D^{20} 1.5028, d_4^{20} 0.9347 [21]; n_D^{20} 1.5017, d_4^{20} 0.9352 [9]; b.p. 115-117° (1.5 mm), n_D^{20} 1.5015, d_4^{20} 0.9352 [22].

SUMMARY

1. A new scheme of irone synthesis was evolved using pinacone and isoprene as the main starting materials.

2. It was shown that the reaction of a mixture of dimethylbutadiene hydrochlorides with isoprene in the presence of stannic chloride as catalyst results in the formation of methylgeranyl chloride in about 16% yield, calculated on the hydrochloride taken or 30.5%, calculated on the hydrochloride reacting.

3. It was established that Krenke's method does not give satisfactory results for the conversion of methylgeranyl chloride into methylcitral. Better results were obtained with Sommle's method – in this case the methylcitral yield was about 20%, calculated on the chloride taken or 40%, considering the unreacted amount.

4. Condensation of methylcitral with acetone was carried out in the presence of sodium sulfite. The pseudoirone prepared contained about 60% of the trans-isomer.

Boron trifluoride was used in the cyclization of pseudoirone into irone.

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* The boron trifluoride was prepared by the method described in [19].

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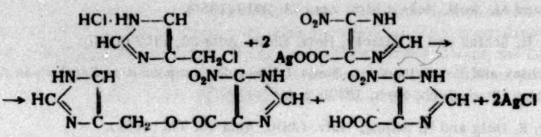
*In Russian.

ESTERS OF 4(5)-NITROIMIDAZOLE-5(4)-CARBOXYLIC ACID

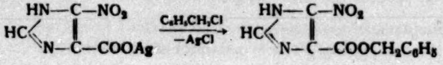
L.P. Kulev and A.M. Rozhkov

The relatively simple and convenient method of preparing 4(5)-nitroimidazolecarboxylic acid, which we developed, based on continuous nitration and oxidation of 4(5)-hydroxymethylimidazole, makes it more accessible and makes it possible to extend the investigations of a series of this acid's derivatives, which as yet have hardly been examined. Thus, of the esters of 4(5)-nitroimidazolecarboxylic acid, the literature only describes the methyl ester, which was prepared from methanol and the nitroacid in the presence of dry hydrogen chloride [2]. It seemed interesting to prepare other esters of this acid and to investigate their properties. As shown by our experiments, the exchange of strong sulfuric acid for hydrogen chloride did not have much effect on the quality and yield of the product. Therefore, we found it more convenient to carry out esterification under normal conditions using sulfuric acid. However, in individual cases, for example in preparing the benzyl ester, a different addition order of the reacting materials had to be followed to avoid resinification of the benzyl alcohol, as explained below. The imidazolylmethyl ester of 4(5)-nitroimidazolecarboxylic acid was prepared from 4(5)-chloromethylimidazole hydrochloride and the silver salt of 4(5)-nitroimidazolecarboxylic acid by the equation



The silver salt required for this reaction was precipitated in the form of fine, yellow crystals by mixing hot alcoholic solutions of silver nitrate and 4(5)-nitroimidazolecarboxylic acid.

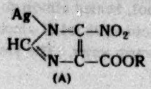
To prove the structure of the salt, which is not described in the literature, the benzyl ester was synthesized by the scheme



It was found to be identical to the ester we obtained from benzyl alcohol and 4(5)-nitroimidazolecarboxylic acid.

4(5)-Chloromethylimidazole hydrochloride was prepared by treating 4(5)-hydroxymethylimidazole hydrochloride with thionyl chloride.

All the esters described here are crystalline substances, which do not form salts even with strong mineral acids; they do not form complexes with picric and chloroplatinic acids. Aqueous solutions of silver nitrate gave white, amorphous precipitates (A) with alcohol solutions of the esters, as in the case methyl 4(5)-nitroimidazolecarboxylate [4].



(A)

Hydrolysis of the esters by heating with a 3% alcoholic KOH solution and subsequently treating the potassium salt with hydrochloric acid, gave 4(5)-nitroimidazolecarboxylic acid and the original alcohol (starting with butyl) in amounts, corresponding to the composition of the ester taken for analysis. In contrast to all the other esters we investigated, imidazolylmethyl 4(5)-nitroimidazolecarboxylate dissolved readily in cold water and with much more difficulty in acetone. It is approximately equal to sulfidine in antibacterial activity, but differs in that it has a bacteriostatic effect on sulfamide-resistant strains of certain microbes. It greatly surpasses the other esters in this connection.

The investigations were carried out in the Tomsk Institute for Research on Vaccines and Serums by N.B. Plakhova under the direction of Prof. S.P. Karpov.

EXPERIMENTAL

Methyl ester (I). 3 g of 4(5)-nitroimidazolecarboxylic acid was placed in 57 ml of anhydrous methyl alcohol, containing 3 g of sulfuric acid (d 1.84). The mixture was heated on a water bath for 1 hour, evaporated down to half its volume and the crystals, which separated on cooling, separated; they were colorless plates with m.p. 212-213° (from boiling water). The yield was 1.9 g (59.6%). The substance was insoluble in cold water, ether, benzene, chloroform and carbon tetrachloride and soluble in hot alcohol and acetone.

Analysis of Esters of 4(5)-Nitroimidazole-5(4)-carboxylic Acid

No. of esters	Formulas of compounds	Found N (%)	Calculated N (%)
I	$C_5H_5O_4N_3$	24.74, 24.67	24.56
II	$C_6H_7O_4N_3$	22.77	22.69
III	$C_7H_9O_4N_3$	20.94, 20.85	21.10
IV	$C_8H_{11}O_4N_3$	19.83	19.71
V	$C_9H_{13}O_4N_3$	18.62, 18.65	18.49
VI	$C_{10}H_{15}O_4N_3$	17.54, 17.59	17.42
VII	$C_{11}H_9O_4N_3$	16.88, 17.09	16.99
VIII	$C_8H_7O_4N_5$	29.32, 29.43	29.53

Data on the analysis of this and the following compounds are given in the table.

Ethyl ester (II). This was prepared similarly to (I) from 3 g of 4(5)-nitroimidazolecarboxylic acid and 53 ml of anhydrous alcohol, containing 3 g of sulfuric acid (d 1.84). The yield was 1.95 g (55.5%).

It formed colorless plates with m.p. 207-208°. It was readily soluble in acetone, hot alcohol and boiling water. It dissolved in dilute alkalis forming a yellow-colored solution. With silver nitrate an alcohol solution of the ester gave a white, amorphous precipitate, which dissolved in nitric acid.

Propyl (III), n-butyl (IV), isoamyl (V) and n-hexyl (VI) esters were prepared similarly to (I) (time of heating 2.5-4 hours) in yields of 52.2, 49.1, 52.6, 47.9% respectively. Melting points: (III) 179-180°, (IV) 182°, (V) 203-204°, (VI) 173-174°. The fine plates were readily soluble in acetone and hot alcohol.

Benzyl ester (VII). 4 g of sulfuric acid was added to 4 g of 4(5)-nitroimidazolecarboxylic acid. The mixture was stirred well until it formed a uniform paste, 76 g of benzyl alcohol slowly added to it and the whole heated on a boiling water bath for 8 hours. Carbon tetrachloride was added to the alcohol solution of the ester, which separated (upper layer), until white crystals ceased to precipitate and it was left to stand. After recrystallization from aqueous acetone, the yield was 3.1 g (49.2%). The fine, colorless crystals had m.p. 200-201°. The substance was soluble in acetone and hot alcohol and insoluble in CCl_4 and other organic solvents.

Imidazolylmethyl ester (VIII). a) Preparation of the silver salt of 4(5)-nitroimidazolecarboxylic acid. 6 g of $AgNO_3$ was dissolved in 150 ml of 98% alcohol, heated almost to boiling. The hot liquid was added with vigorous stirring to a hot solution of 5 g of nitroacid in 95 ml of alcohol. The yellow crystals, which precipitated on cooling, were filtered off and washed with warm water. The yield was 7.9 g (94%). The salt was insoluble in water; it decomposed on heating above 300°.

b) Preparation of the ester. 5.1 g of the silver salt of the nitroacid was suspended in 75 ml of anhydrous methyl alcohol, 1.4 g of 4(5)-chloromethylimidazole hydrochloride introduced and the mixture heated for 3 hours on a water bath. The silver chloride precipitate was filtered off and washed with methyl alcohol and the filtrate evaporated to dryness. To isolate the ester from the mixture, the dry residue was dissolved in ethyl alcohol with heating and CCl_4 or $(C_2H_5)_2O$ added until no more white precipitate formed. The yield was 2.1 g (91.3%). The fine, colorless plates had m.p. 153-154° (from a mixture of alcohol and ether). The substance was readily soluble in water and hot alcohol, and slightly soluble in acetone; it did not dissolve in ether, benzene, carbon tetrachloride and chloroform.

SUMMARY

1. We prepared the ethyl, n-propyl, n-butyl, isoamyl, n-hexyl, benzyl and imidazolylmethyl esters of 4(5)-nitroimidazole-5(4)-carboxylic acid. It was shown that the esters of this acid, in contrast to many other imidazole derivatives, did not form salts and complexes with mineral and organic acids.

2. Experiments in vitro established that of all the esters investigated, the imidazolylmethyl 4(5)-nitroimidazolecarboxylate had the strongest bacteriostatic effect on sulfamide-resistant strains of certain microbes.

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SOME ETHERS OF 4(5)-HYDROXYMETHYLIMIDAZOLE

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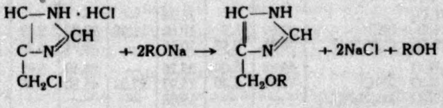
Imidazole derivatives have a considerable interest as substances which, in many cases, have valuable physiological properties. Thus, for example, histidine and histamine have long been known in this connection and have been used as medicines with diverse effects. Some sulfur-containing compounds of the imidazole series, prepared by P.M. Kochergin and M.N. Shchukina [1, 2],have shown a considerable antitubercular bacillus activity in experiments in vitro. A large group of imidazole derivatives, among them the esters of 2-hydroxymethylbenzimidazole, were investigated by B.A. Porai-Koshits, L.S. Efros et al. [3-6]. Of the esters of 4(5)-hydroxymethylimidazole, the 4-amino- and 4-butylaminobenzoates are of interest as they possess local anesthetic activity [7]. Ruoff and Scott [8] prepared a series of ethers of 4(5)-hydroxymethylimidazole, containing both aliphatic and aromatic radicals. On testing these ethers for antihistamine activity, they were found to have a low activity. Ethers of 4(5)-hydroxyethylimidazole, analogous to them, had a contrary effect, i.e., they had a histamine-type of activity which was especially strong in the β-naphthyl ether [9].

The purpose of this work was to prepare some ethers of 4(5)-hydroxymethylimidazole and to find out the relation between their structure and pharmacological activity.

The ethers were prepared from 4(5)-chloromethylimidazole hydrochloride and the corresponding alcoholate by the scheme



To prepare chloromethylimidazole, 4(5)-hydroxymethylimidazole was used as the starting material and was in its turn prepared from invert sugar by a method developed by one of us together with A.E. Onishchuk [10].

The free ethers of the naphthalene series were crystalline substances, the rest were sirupy liquids, which hardened very slowly to a glassy mass on standing in a vacuum desiccator.

They all gave salts with hydrochloric acid which dissolved readily in water and alcohol; with picric acid they gave picrates with a composition of 1:1 and 1:2.

The ethers were tested as hydrochlorides in the pharmacological laboratories of the Tomsk Institute of Medicine by Prof. A.S. Saratikov. The β-naphthyl ether of 4(5)-hydroxymethylimidazole was found to have the strongest hypotensive activity and in this connection it is closest to histamine. In contrast to the β-naphthyl ether, the α-naphthyl ether induces a sharp increase in blood pressure. The phenyl and nitrophenyl ethers also have considerable hypotensive activity, and the latter, especially the ortho- and para-isomers, are noticeably weaker than the former. The hypotensive activity of the p-aminophenyl ether increases with the reduction of its nitro group. Alkylation of the amino groups of the side chain results in substantial changes in the physiological properties of the ether. Thus, the β-aminoethyl ether of 4(5)-hydroxymethylimidazole has a histamine-like activity, while its alkylated derivatives, primarily the diethylaminoethyl ether, on the contrary has a rather strong antihistamine activity.

EXPERIMENTAL

I. β-Naphthyl ether of 4(5)-hydroxymethylimidazole. 1.37 g of metallic sodium was gradually added to 100 ml of anhydrous alcohol. 8.66 g of β-naphthol in 50 ml of anhydrous alcohol was added to the solution of alcoholate obtained, the solution stirred for two hours and an alcohol solution of 4(5)-chloromethylimidazole hydrochloride added. The mixture was heated on a water bath at 50° for 1 hour and left to stand. It was filtered, the filtrate evaporated in vacuum until it became sirupy, 50 ml of 2 N hydrochloric acid added and the mixture stirred. The excess β-naphthol was extracted with ether. The ether hydrochloride precipitated from the acidified solution as white crystals with m.p. 266-268°. The yield was 3.0 g (38.2%). It was readily soluble in water and alcohol. On combining an aqueous solution of the hydrochloride with diazotized sulfanilic acid, an orange-red spot was produced on filter paper. Data on the analysis of this ether, its hydrochloride and picrate and also all the compounds described below are given in the table.

Analysis of the Ethers of 4(5)-Hydroxymethylimidazole and Their Hydrochlorides and Picrates

No. of ether	Formula of compound	Found (%) C	Found (%) H	Found (%) N	Found (%) Cl	Calculated (%) C	Calculated (%) H	Calculated (%) N	Calculated (%) Cl
I	$C_{14}H_{12}N_2O$	74.58	5.19	12.43	—	75.0	5.35	12.5	—
	$C_{14}H_{12}N_2O \cdot HCl$	64.38	5.2	11.05	13.56	64.51	4.99	10.71	13.62
	$C_{14}H_{12}N_2O \cdot C_6H_3N_3O_7$	52.68	3.27	15.9	—	52.92	3.31	15.45	—
II	$C_{14}H_{12}N_2O$	74.50	5.26	12.7	—	75.0	5.35	12.5	—
	$C_{14}H_{12}N_2O \cdot HCl$	—	—	10.51	13.7	—	—	10.71	13.62
	$C_{14}H_{12}N_2O \cdot C_6H_3N_3O_7$	—	—	15.43	—	—	—	15.45	—
III	$C_{10}H_9N_3O_3 \cdot HCl$	46.70	4.0	16.17	14.05	46.96	3.91	16.43	13.89
	$C_{10}H_9N_3O_3 \cdot C_6H_3N_3O_7$	42.67	2.49	19.02	—	42.85	2.68	18.75	—
IV	$C_{10}H_9N_3O_3 \cdot HCl$	46.82	3.86	16.77	14.15	46.96	3.91	16.43	13.89
	$C_{10}H_9N_3O_3 \cdot C_6H_3N_3O_7$	42.24	2.69	18.54	—	42.85	2.68	18.75	—
V	$C_{10}H_9N_3O_3$	54.58	4.2	19.0	—	54.79	4.11	19.17	—
	$C_{10}H_9N_3O_3 \cdot HCl$	46.79	3.99	16.65	14.07	46.96	3.91	16.43	13.89
	$C_{10}H_9N_3O_3 \cdot C_6H_3N_3O_7$	42.67	2.89	18.75	—	42.85	2.68	18.75	—
VI	$C_{10}H_8N_4O_5$	—	—	21.23	—	—	—	21.21	—
	$C_{10}H_8N_4O_5 \cdot HCl$	39.65	3.2	18.60	11.96	39.93	2.99	18.63	11.81
	$C_{10}H_8N_4O_5 \cdot C_6H_3N_3O_7$	38.91	2.49	20.18	—	38.94	2.23	19.87	—
VII	$C_{10}H_{11}N_3O$	63.18	6.09	22.26	—	63.49	5.82	22.22	—
	$C_{10}H_{11}N_3O \cdot 2HCl$	45.59	5.20	15.97	27.22	45.80	4.96	16.03	27.09
	$C_{10}H_{11}N_3O \cdot 2C_6H_3N_3O_7$	—	—	19.48	—	—	—	19.47	—
VIII	$C_6H_{11}N_3O \cdot 2C_6H_3N_3O_7$	35.89	2.79	21.21	—	36.06	2.83	21.03	—
	$C_6H_{11}N_3O \cdot 2HCl$	33.70	6.08	19.45	33.7	33.64	5.14	19.62	33.17
IX	$C_8H_{15}N_3O \cdot 2C_6H_3N_3O_7$	—	—	20.34	—	—	—	20.09	—
	$C_8H_{15}N_3O \cdot 2HCl$	—	—	17.28	28.89	—	—	17.35	29.33
X	$C_{10}H_{19}N_3O \cdot 2C_6H_3N_3O_7$	40.19	4.09	19.07	—	40.3	3.81	19.23	—
	$C_{10}H_{19}N_3O \cdot 2HCl$	44.23	6.04	15.59	26.57	44.60	7.43	15.61	26.39

The free β-naphthyl ether was prepared from its hydrochloride by neutralizing the solution with sodium bicarbonate. It was a fine, crystalline, white powder with m.p. 108-110° (from alcohol). The picrate was prepared by adding a saturated aqueous solution of picric acid to an aqueous solution of the ether hydrochloride. The solidified oil was readily ground to a powder, which was soluble in hot water. The m.p. was 173-174°.

II. α-Naphthyl ether of 4(5)-hydroxymethylimidazole and its hydrochloride and picrate were prepared similarly to (I). The free ether was a light brown, fine, crystalline powder. The yield was 4.4 g (65.38%). The m.p. was 69-70° (from 50% alcohol). The ether hydrochloride was a white powder with m.p. 78-80°. It was very hygroscopic. The picrate was a yellow powder with m.p. 120-122°; it was soluble in acetone.

III. o-Nitrophenyl ether of 4(5)-hydroxymethylimidazole. 15 g of o-nitrophenol was dissolved in 40 ml of alcohol and an alcohol solution of 4.5 g of sodium hydroxide added. Solutions of 8.5 g of o-nitrophenolate in 50 ml of anhydrous alcohol and 3.82 g of 4(5)-chloromethylimidazole hydrochloride in 80 ml of anhydrous alcohol were mixed. The mixture was heated on a water bath at 50° for 1 hour, left to stand for 4-5 hours, filtered and the filtrate made slightly acid and evaporated in vacuum. 30 ml of water and 7 ml of 6 N hydrochloric acid was added to the sirup, which was stirred and treated several times with ether to remove excess nitrophenol, and the water-acid layer evaporated in vacuum. After standing for a long time in a vacuum desiccator, the thick sirup set to a glassy mass, which was readily ground to a powder. The ether hydrochloride was hygroscopic and rapidly deliquesced in air. The yield was 3.8 g (62%). The m.p. was 65°. It was readily soluble in water and alcohol; it did not dissolve in benzene, ether and chloroform. The ether picrate was prepared from an aqueous solution of the hydrochloride by precipitation with a saturated solution of picric acid. It was a yellow powder with m.p. 135-140°.

IV. m-Nitrophenyl ether of 4(5)-hydroxymethylimidazole was prepared similarly to (III) from 9.85 g of m-nitrophenolate and 3.82 g of 4(5)-chloromethylimidazole hydrochloride, as its hydrochloride. The yield was 2.1 g (36.2%). The m.p. was 168-169°. The ether picrate had m.p. 181-182° (with decomposition).

V. The p-nitrophenyl ether of 4(5)-hydroxymethylimidazole was prepared similarly to (IV). The yellow powder had m.p. 123-124°. The yield was 1.19 g (21.97%). It was readily soluble in alcohol and almost insoluble in water. The hydrochloride of the ether had m.p. 181-183°. The picrate of the ether had m.p. 170-175°.

VI. The 2,4-dinitrophenyl ether of 4(5)-hydroxymethylimidazole was prepared similarly to (III) from 11.2 g of dinitrophenolate and 3.82 g of 4(5)-chloromethylimidazole hydrochloride. The free ether was very hygroscopic. It was readily soluble in water and alcohol. The ether hydrochloride had m.p. 70-72°. The ether picrate had m.p. 158°.

VII. p-Aminophenyl ether of 4(5)-hydroxymethylimidazole. 25 g of iron filings was added to 20 ml of 0.05 N hydrochloric acid and the mixture well stirred. At the end of the reaction, the mixture was heated to 60-65° and 2.19 g of the p-nitrophenyl ether of 4(5)-hydroxymethylimidazole hydrochloride added to it. The reduction proceeded for 8 hours with stirring. The reaction mixture was filtered, the residue washed 2-3 times with water and the ether extracted from it with hot alcohol. The free ether formed prisms with m.p. 112-114°. The yield was 0.9 g (57%). The ether hydrochloride had m.p. 213° (from water). The ether picrate had m.p. 204-206°. It was soluble in acetone.

VIII. Aminoethyl ether of 4(5)-hydroxymethylimidazole. 2.3 g of metallic sodium was added in small portions to 15 g of aminoethanol. The alcoholate obtained was dissolved in anhydrous alcohol and an alcohol solution of 7.65 g of 4(5)-chloromethylimidazole hydrochloride added. The mixture was heated at 40-45° for 30 minutes and left to stand. The excess alcoholate was decomposed with hydrochloric acid, the solution filtered and the liquid evaporated in vacuum to a thick sirup. The sirup was diluted with water and the ether isolated from it as the picrate. The yield was 17 g (91.9%). The m.p. was 108-110°. The ether hydrochloride was prepared from the picrate. 2 g of the picrate was added to a heated mixture of 5 ml of water, 2 ml of hydrochloric acid (d 1.18) and 10 ml of benzene. The benzene was separated and the water-acid layer treated with benzene 3-4 more times and evaporated in vacuum. The ether hydrochloride formed colorless crystals with m.p. 165°. It was very hygroscopic. The free ether (a glassy mass) was not analyzed.

IX. Dimethylaminoethyl ether of 4(5)-hydroxymethylimidazole was prepared similarly to (VIII) from an alcohol solution of the alcoholate and 4(5)-chloromethylimidazole hydrochloride. The free ether was a sirupy liquid. It was extremely hygroscopic. The ether picrate had m.p. 85-90°. The yield was 23.2 g (77.19%). It was soluble in water, alcohol and acetone. The ether hydrochloride formed colorless crystals; they were very hygroscopic.

X. The diethylaminoethyl ether of 4(5)-hydroxymethylimidazole was prepared similarly to (IX). The free ether was a glassy mass, which was very hygroscopic and readily soluble in water and alcohol. The ether picrate had m.p. 181-183°. It was slightly soluble in acetone and insoluble in water and alcohol. The ether hydrochloride had m.p. 88-90°. It was readily soluble in water and alcohol.

SUMMARY

1. Some ethers of 4(5)-hydroxymethylimidazole and their picrates and hydrochlorides were prepared.

2. The physiological activity of the compounds investigated was relatively low. It was established that the β-naphthyl ether has the strongest histamine-like activity and the diethylaminoethyl ether of 4(5)-hydroxymethylimidazole has the strongest antihistamine activity.

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FLUORINE-CONTAINING DERIVATIVES OF DIMETHYLAMINOAZOBENZENE

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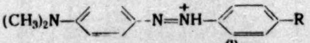
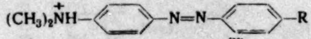
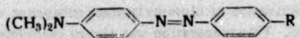
In order to study the effect of fluorine-containing substituents on the properties and color of azo dyes, we synthesized a series of fluorine derivatives of dimethylaminoazobenzene and compared their colors in neutral and acidic solutions with those of the corresponding compounds without fluorine. As is known, addition of acid to aminoazo compounds causes a deepening of color. This is explained by the formation of a cation (I), in which the cationic charge is capable of moving readily along the chain of the configuration. As Hantzschhas shown [1], at the same time a greater amount of cation (II) is formed, where the ionic charge is fixed at the dimethylamino group, and its absorption is very similar to that of the corresponding azo derivative, without the amino group.


(I)


(II)

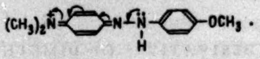
The substituent R in the position para to the azo group has an effect on the color both of the bases and the salts of aminoazo compounds. Table 1 gives the results of measurements of absorption maxima and molecular extinctions of the dyes we synthesized, in neutral alcohol and in alcohol with hydrochloric acid (2 volumes of alcohol to one of hydrochloric acid with specific gravity 1.19). For comparison the same data are given for known aminoazo compounds.

TABLE 1

Dyes 

R	λ_{max} in alcohol (in mμ)	$\epsilon \cdot 10^{-4}$	λ_{max} in alcohol + + HCl (in mμ)	$\epsilon \cdot 10^{-4}$
H [2] . . .	407	2.80	518	4.60
$N(CH_3)_2$ . .	—	—	Monosalt with CH_3COOH ~ 650 [3]	—
OCH_3 [3—5]	407	2.86	555	2.31
OCF_3 . . .	419	3.05	512	3.76
SCH_3 . . .	420	3.3	555	3.08
SCF_3 . . .	432	3.13	516	4.91
SO_2CH_3 . .	445	3.15	505	4.80
SO_2CF_3 . .	476	3.50	500	6.50
CH_3 [2, 5] .	408	2.80	524	3.80
CF_3	430	2.84	505	3.60
NO_2 [6] . .	475	3.20	508	5.68
$SeCH_3$ . .	420	3.39	545	3.66

As can be seen from the data in Table 1, the absorption maxima of salts of aminoazo compounds are displaced more towards longer wavelengths the more electropositive the substituent introduced in the position para to the azo group. This is due to the fact that electropositive substituents create an electronic pressure on the nitrogen atom of the azo group and hence promote the even distribution of electron density along the chain of the configuration; electronegative substituents behave in the opposite way, for example,



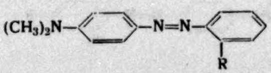
Electropositive substituents have very little effect on the color of the aminoazo bases. In contrast to this, electronegative substituents sharply displace the absorption maximum towards longer wavelengths, and the more electronegative the substituents introduced in the position para to the azo group, the stronger the displacement.

The absorption maxima of salts of azo dyes with fluorine-containing substituents CF_3S- and CF_3O- are displaced towards shorter wavelengths in comparison with those of the corresponding methoxy and methylmercapto derivatives. This shows that their electron donor character is weaker; the CF_3SO_2-group is similar to a nitro group in its effect on the absorption of the base of an azo dye and its salt; the CH_3SO_2-group, as might be expected, is a weaker electronegative substituent than the CF_3SO_2-group.

As can be seen from the results obtained, knowing the electronic characteristics of a substituent, it is possible to foretell the color of corresponding derivatives of dimethylaminoazobenzene and their salts and, contrarily, from this color it is possible to obtain some idea of the electronic nature of the substituent.

TABLE 2

Dyes



R	λ_{max} in alcohol (in mμ)	$\epsilon \cdot 10^{-4}$	λ_{max} in alcohol + HCl (in mμ)	$\epsilon \cdot 10^{-4}$
CF_3	425	2.98	479	0.08
CH_3 [2]	410	2.70	520	1.00
NO_2 [6]	440	2.68	500	1.11

We also synthesized a derivative of dimethylaminoazobenzene containing a trifluoromethyl group in the position ortho to the azo group. This preparation was almost completely decolorized when treated with acid which, apparently, can be explained by the large volume of the trifluoromethyl group and its electronegative character hindering the addition of a proton to the nitrogen atom of the azo group and the salt being formed at the dimethylamino group. Table 2 gives the results of measurements of absorption maxima and extinctions of three of such compounds.

As can be seen from the data in Table 2, the methyl group, which is effective only through its large volume, and the nitro group, which attracts the electrons from the nitrogen atom of the azo group, but does not offer much steric hindrance, lower the absorption intensity of dye salts to a lesser degree than the CF_3-group.

EXPERIMENTAL

The intermediates required for the synthesis of the azo dyes were prepared by the following methods. p-Aminophenyl methyl sulfide [7], p-aminophenyl trifluoromethyl sulfide [8], p-aminophenyl trifluoromethyl ether [9], p-aminophenyl trifluoromethyl sulfone [10], o-aminobenzotrifluoride [11] and p-aminobenzotrifluoride [12] were synthesized by methods described in the literature.

p-Aminophenyl methyl sulfone. A solution of 1.8 g of p-acetylaminophenyl methyl sulfide in 10 ml of acetic acid was heated with 6 ml of 30% hydrogen peroxide for 2 hours, poured into a porcelain basin and evaporated to dryness. The product obtained was crystallized from water. The yield was 1.5 g (71%). The m.p. was 185-186°.

1.5 g of p-acetylaminophenyl methyl sulfone was boiled under reflux until it dissolved in 8 ml of 15% hydrochloric acid. The amine was precipitated by adding 20% sodium hydroxide solution, filtered off and crystallized from alcohol. The yield was 1 g (83%); the m.p. of 134-135° agreed with that in the literature [13].

p-Aminophenyl methyl selenide. 2.8 g of p-nitrophenyl methyl selenide [14] was dissolved in 7 ml of alcohol and gradually added to a solution of 15 g of stannous chloride in 26 ml of concentrated hydrochloric acid at 60-70°. The solution was heated on a water bath for 1 hour, cooled and poured onto a mixture of ice and sodium hydroxide solution. The amine was extracted with ether. The ether was distilled off. The product was distilled in vacuum. The b.p. was 103-105° (5 mm). The acetyl derivative had m.p. 99-100°.

Found %: N 6.40, 6.44. $C_9H_{11}ONSe$. Calculated %: N 6.14.

TABLE 3

Dyes $(CH_3)_2N-C_6H_4-N=N-C_6H_4R$

R	Yield (in %)	Melting point	Empirical formula	Calculated % N	Found % N
p-SCH_3	83	175—176°	$C_{15}H_{17}N_3S$	15.5	15.21, 15.33
p-SCF_3	80	169—170	$C_{15}H_{14}N_3SF_3$	12.92	13.05, 13.16
p-SO_2CH_3	60	223—224	$C_{15}H_{17}O_2N_3S$	13.8	13.60, 13.71
p-SO_2CF_3	82	175—176	$C_{15}H_{14}O_2N_3SF_3$	11.76	11.61, 11.63
p-OCF_3	75	131—132	$C_{15}H_{14}ON_3F_3$	13.59	13.29, 13.42
p-CF_3	75	175	$C_{15}H_{14}N_3F_3$	14.33	14.03, 14.08
p-$SeCH_3$	80	175—176	$C_{15}H_{17}N_3Se$	13.2	13.27, 13.42
o-CF_3	50	120	$C_{15}H_{14}N_3F_3$	14.33	14.20, 14.23

We synthesized the azo dyes not described in the literature by the following standard method. 1 g of the appropriate amine was mixed with 4 ml of concentrated hydrochloric acid and 16 ml of water and diazotized with the calculated amount of sodium nitrite at 0° with stirring. The solution was neutralized with sodium acetate, filtered and added to a solution of the calculated amount of dimethylaniline in 4 ml of 50% acetic acid. The following day the dye was filtered off and crystallized from alcohol.

The yields, melting points and analysis results of the dyes synthesized are given in Table 3.

SUMMARY

We synthesized a series of fluorine derivatives of dimethylaminoazobenzene. The absorption spectra and extinctions were measured in neutral and acidic solutions.

It was shown that the absorption maxima of salts of dimethylaminoazobenzene with fluorine-containing substituents are displaced towards shorter wavelengths in comparison with the corresponding compounds without fluorine.

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SOME N-SUBSTITUTED β-CHLOROPROPIONAMIDES

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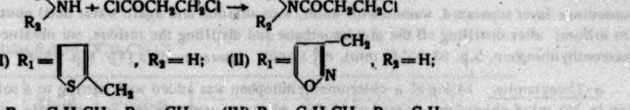
Recently we described the preparation of a series of N-benzyl-β-chloropropionamides, containing various substituents in the aromatic nucleus [1]. Pharmacological tests of the compounds obtained [2] showed that some of them are highly efficient antispasmodics (chloracon, chibicon). In order to find further antispasmodics in this series of compounds and to elucidate the relation between physiological activity and structure, we undertook the synthesis of some N-substituted β-chloropropionamides. We prepared two heterocyclic isologs of N-benzyl-β-chloropropionamide (chloracon), namely N-(α-thenyl)-β-chloropropionamide (I) and N-[isoxazolyl-(3)-methyl]-β-chloropropionamide (II). To find the effect of substituting the hydrogen in the N-benzylamide grouping, we prepared N-methyl-N-benzyl-β-chloropropionamide (III) and N-phenyl-N-benzyl-β-chloropropionamide (IV). In addition, N-(β-phenylethyl)-β-chloropropionamide (V) and N-benzohydryl-β-chloropropionamide (VI) were synthesized.



$$\begin{matrix}R_1\\R_2\end{matrix}\!\!>NH + ClCOCH_2CH_2Cl \rightarrow \begin{matrix}R_1\\R_2\end{matrix}\!\!>NCOCH_2CH_2Cl$$

(I) $R_2 = H$; (II) $R_2 = H$;

(III) $R_1 = C_6H_5CH_2,\ R_2 = CH_3$; (IV) $R_1 = C_6H_5CH_2,\ R_2 = C_6H_5$;
(V) $R_1 = C_6H_5CH_2CH_2,\ R_2 = H$; (VI) $R_1 = (C_6H_5)_2CH,\ R_2 = H$.

We prepared all the compounds, except (IV), by acylation of the appropriate amines with β-chloropropionyl chloride in the presence of alkali in an aqueous medium, as described for the synthesis of various N-benzylamides [3] and used by us for the preparation of substituted N-benzyl-β-chloropropionamides [1]. Compound (IV) was prepared in chloroform and excess amine was used to combine with the hydrogen chloride. An attempt to obtain the pyridine isolog – N-[pyridyl-(3)-methyl]-β-chloropropionamide was unsuccessful. In acylating pyridyl-(3)-methylamine with β-chloropropionyl chloride even under mild conditions and using excess amine to combine with the hydrogen chloride, we consistently obtained a substance, which corresponded to the required amine in composition but whose properties (presence of a multiple bond and ionic chlorine, solubility in water and insolubility in ether) showed that actually the reaction product was, most probably, the hydrochloride of N-pyridylmethylacrylamide.

Some of the amines required as starting materials for synthesizing the compounds (I-VI), were prepared by known methods. Benzohydrylamine was prepared from benzohydryl bromide through the urotropin salt by the method we developed for substituted benzylamines [1]. Although the yield of benzohydrylamine obtained by this method was moderate (40%), this method of preparing it in the laboratory has its advantages. To obtain α-thenylamine, starting with thiophen we prepared α-chloromethylthiophen, changing somewhat the usual method of thiophen chloromethylation, and the chloride obtained was converted into the amine through the urotropin salt. There were difficulties in preparing pyridyl-(3)-methylamine, whose synthesis is not clearly described in the literature. We prepared this amine by hydrogenating nicotinonitrile over Raney nickel at room temperature, the yields fluctuated greatly from experiment to experiment.

N.V. Kaverina carried out the pharmacological tests on the N-substituted β-chloropropionamides in the pharmacological section of our institute. In connection with antispasmodic activity – compounds (I), (II) and (VI) were found to be inactive, compounds (III) and (IV) had a slight activity. Compound (V) was found to have low toxicity and high efficiency especially for tremors and tetanus convulsions. In addition, (III) and (V) were found to have a noticeable ganglion blocking effect, while (IV) had a soporific effect. Thus, the substitution of the benzene nucleus of chloracon by thiophen or isoxazole completely eliminated antispasmodic activity; substitution of hydrogen in the benzylamide grouping strongly decreased it and simultaneously changed the character of the pharmacological effect. The substitution of the benzyl by the benzohydryl residue completely eliminated the activity; an analogous effect is known also for a series of antihistamine substances [4].

EXPERIMENTAL

N-Methylbenzylamine was prepared from the data in [5] in 80% yield and had b.p. 62-63° (6 mm), n_D^{20} 1.5210.

β-Phenylethylamine was prepared by hydrogenation of benzyl cyanide over Raney nickel in anhydrous alcohol at room temperature. The yield was 64.5%, b.p. 65-70° (5 mm) n_D^{21} 1.5290.

Isoxazolyl-(3)-methylamine was prepared from the data in [6] in 42% yield and had b.p. 60-61° (4 mm), n_D^2 1.4890.*

α-Chloromethylthiophen. In contrast to established methods, the chloromethylation of thiophen was carried out by treatment with paraformaldehyde in dichloroethane. A solution of 15 g of thiophen in 60 ml of dichloroethane was placed in a flask fitted with a stirrer and a thermometer and a current of dry hydrogen chloride was passed in for 15 minutes. Then 7 g (20% excess) of paraformaldehyde was added and while the temperature of the mixture was kept at 2-10°, a fast current of hydrogen chloride passed in. When heat was no longer evolved, the mixture was saturated with hydrogen chloride for a further 1.5 hours, after which water was added and the dichloroethane layer separated, washed with water, soda solution and again water until neutral and dried over sodium sulfate; after distilling off the dichloroethane and distilling the residue, we obtained 11 g (47%) of α-chloromethylthiophen, b.p. 53-55° (6 mm), n_D^{20} 1.5605. Literature data [7]: b.p. 78-82° (18 mm).

α-Thenylamine. 14.5 g of α-chloromethylthiophen was added with stirring to a solution of 15.5 g of urotropin in 125 ml of chloroform, heated to 50-70°, when the urotropin salt immediately precipitated in a crystalline form. The mixture was kept overnight and then the precipitate of urotropin salt filtered off (29 g) and decomposed by heating on a water bath with 150 ml of a mixture of alcohol and concentrated hydrochloric acid (3 : 1). After separating off the ammonium chloride precipitate, the filtrate was reduced to small volume, treated with an aqueous solution of alkali, the base extracted with ether and the extracts dried over potash and distilled. We obtained 5.2 g (41%) of α-thenylamine with b.p. 49-50° (4 mm) n_D^{19} 1.5660. Literature data [8]: b.p. 77° (16 mm), n_D^{15} 1.5678.

Benzohydrylamine. 29.5 g of diphenylbromomethane, dissolved in 50 ml of chloroform, was added with stirring to a solution of 20.6 g of urotropin in 150 ml of chloroform at 40-50°; after 15-20 minutes the urotropin salt began to separate. After heating the mixture for 3 hours, it was left overnight and 50 g of urotropin salt separated. After decomposing it with a mixture of hydrochloric acid and methanol as described above and separating off the ammonium chloride, the filtrate was concentrated in vacuum, the crystalline residue carefully treated with an aqueous solution of alkali, the oily base which separated extracted with ether and the ether extract extracted with hydrochloric acid. After evaporating the acid extract on a water bath, we obtained 10.7 g (40.9%) of benzohydrylamine hydrochloride as lustrous, colorless crystals with m.p. 286-287°. Literature data [9]: m.p. 280°.

Found %: Cl 15.83, 15.72. $C_{13}H_{14}NCl$. Calculated %: Cl 16.13.

β-Aminomethylpyridine. This was prepared by hydrogenating nicotinonitrile over Raney nickel in anhydrous alcohol at room temperature until 2 moles of hydrogen had been absorbed. The hydrogenation was complicated by condensation processes and the formation of high-boiling fractions, which caused the yield of β-aminomethylpyridine to fluctuate considerably (15-40%). The substance had b.p. 75-78° (4 mm), n_D^{19} 1.5510. Literature data [10]: b.p. 103° (11 mm).

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*As in original – Publisher's note.

The hydrochloride was prepared by saturating an ether solution of the base with hydrogen chloride, after which it was recrystallized from anhydrous alcohol to form colorless plates with m.p. 165-167°.

Found %: Cl 24.75, 24.90. $C_6H_9N_2Cl$. Calculated %: Cl 24.53.

The dihydrochloride was prepared by evaporating down an aqueous solution of the base in hydrochloric acid and after recrystallization from anhydrous alcohol it formed colorless crystals with m.p. 221-223°. Literature data [10]: m.p. 224°.

Found %: Cl 38.88, 39.10. $C_6H_{10}N_2Cl_2$. Calculated %: Cl 39.18.

N-Substituted-β-chloropropionamides (I-VI). With vigorous stirring and cooling to 3-8°, to a solution or an emulsion of 0.1 mole of amine in 30-40 ml of water (with the addition of a few milliliters of alcohol where necessary) we simultaneously added dropwise 0.103 moles of β-chloropropionyl chloride and a solution of 0.105 moles of sodium hydroxide in 10 ml of water, so that at the end of the reaction the pH of the mixture was about 8.0. The mixture was stirred for 1 hour and the precipitate of β-chloropropionamide filtered off and recrystallized from anhydrous alcohol. The compound (III) turned out to be liquid and was extracted with ether and purified by distillation in high vacuum. In the case where the amine hydrochloride was acylated (in the preparation of VI), the aqueous solution of the hydrochloride was first neutralized with alkali until the base separated and the emulsion obtained was treated as described above. Due to the complete insolubility of benzylaniline in water, the compound (IV) was prepared by a different method. With stirring, 12.7 g of β-chloropropionyl chloride was added to a solution of 36.6 g of benzylaniline in 70 ml of chloroform while the mixture was kept at 30-40°, the mixture was stirred for 2 hours at room temperature, the precipitate of benzylaniline hydrochloride filtered off and the alcohol evaporated off from the filtrate in vacuum. The oily residue crystallized after drying over phosphorus pentoxide in vacuum and was recrystallized from alcohol. Data on the substances obtained are given in the table.

Amides $R_1R_2NCOCH_2CH_2Cl$

Substance No.	Yield (in %)	Melting point	N (%)		Cl (%)	
			found	calc.	found	calc.
(I)	75.5	100—101°	6.60, 6.46	6.87	17.15, 17.46	17.41
(II)	73	76—78	14.52, 14.65	14.85	19.04, 18.58	18.80
(III)	76	—*	6.59, 6.56	6.61	16.53, 16.56	16.75
(IV)	82	64—65	5.20, 5.21	5.11	12.57, 12.65	12.96
(V)	72	58—59.5	6.67, 6.59	6.61	16.64, 16.85	16.75
(VI)	60	173—175	4.80, 4.90	5.12	13.07, 13.17	12.95

*B.p. 95-96° (0.05 mm), n_D^{21} 1.5430.

SUMMARY

We described the preparation of some N-substituted β-chloropropionamides and on the basis of pharmacological tests, we discussed the problem of the relation of antispasmodic activity to structure in this series of compounds.

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